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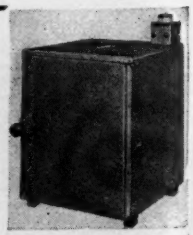

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THE AGRICULTURAL RESEARCH COUNCIL

THE report of the Agricultural Research Council for 1956–57* covers the first year of operations under the Agricultural Research Act, 1956, which made the Council directly responsible to Parliament and not to the Treasury for its expenditure on agricultural research. Under these new arrangements the Council has taken over responsibilities that the Ministry of Agriculture had in financing State-aided agricultural research centres in England and Wales. The total vote by Parliament to the Agricultural Research Fund for 1956–57 was £3,626,000, and this was allocated to a very wide range of research, much of it of a fundamental nature.

One very pleasing feature of the work is the substantial number of 'research units' which are set up in close association with universities and usually with the head of the university department as its honorary director. Men like Prof. F. G. Gregory, with his Research Institute of Plant Physiology at the Imperial College of Science and Technology, London, and Prof. K. Mather, with his Unit of Biometrical Genetics at Birmingham, are assisted by the provision of staff and facilities to develop research programmes which could not otherwise be undertaken. In addition, direct grants are given to universities to enable research on specific projects of shorter duration. Nearly every university in Great Britain is represented in this list, and virtually every science basic to agriculture is included. Then there are the research studentships and fellowships, numbering 75 in all, to promote the training of research workers, mainly in universities. By following such a policy not only is the Council safeguarding the supply of trained staff for the large State-aided or financed research institutes which are its main concern, but also it is helping in providing the stimulus of lively research at teaching centres.

The list of research institutes is a long and impressive one. At the head of the list is Rothamsted, which was once financed by a private endowment from its founder, Sir John Lawes. Now 90 per cent of its funds are provided by the Agricultural Research Fund. Plant breeding is very well catered for, and there are three major institutes concerned with this work, while there are other centres with plant breeding departments. Here, one detects a certain lack of balance, for considerably less emphasis is placed on animal breeding for, apart from poultry (which is well served), there is only one major organization concerned with this very important field. It is not suggested that plant breeding should receive less attention so that animals should receive more, but that animal-breeding studies should, in their own right, receive more help, for animal production constitutes the major part of total agricultural production in Great Britain. Though the beef industry is one of the most important branches of farming, apart from some reference to the genetics of beef and milk production in dual-purpose cattle at the University of Edinburgh and carcass-quality studies at Cambridge, there appears to be little concern for the future of the roast beef of England.

On the other hand, the dairy industry is well catered for with two large institutes at Reading and Ayr, and here again this emphasizes the need for the projected Meat Research Institute to co-ordinate and assist the limited amount of research which is being undertaken with meat animals.

Another major deficiency of immediate concern is the poverty of research into farm buildings. The Agricultural Research Council has a special committee on this, headed by the Council's chairman, but so far matters do not appear to have progressed much beyond the committee stage. The State, however, has committed itself to a very expensive farm improvement scheme; but there is not the basic information on building design to ensure the thrift of housed stock or to secure a fuller economy of labour.

But one must not judge the work of the Council by such deficiencies, for there is so much that is good that has been achieved. There is the better understanding of husbandry control of internal parasites that has come out of the work of the Grassland Research Station at Hurley; there is the Wye College contribution on MCPB to give a herbicide which does not injure clovers; the new winter oat Powys that Aberystwyth has bred, and a dozen more instances of really valuable advances. Especially is this true on the veterinary side, where Britain preserves its long-established leadership. The value of this work in one field may be instanced by a quotation from the report on the Moredun Institute: "Not more than thirty years ago there were in Britain nineteen major diseases of the sheep, of which the causes were unknown. To-day, in eighteen of these diseases the cause has been demonstrated and in fourteen of them specific means for cure or prevention have been evolved". This is a fine record, and one would imagine that these advances in controlling sheep diseases alone have effected an annual saving more than sufficient to fund the whole cost of the Agricultural Research Council's work.

* Committee of the Privy Council for Agricultural Research. Report of the Agricultural Research Council for the year 1956–57. Pp. iv+152. (Cmnd. 432.) (London: H.M. Stationery Office, 1958.) 7s. net.

SCIENTIFIC DEVELOPMENT AND THE UNIVERSITIES

Technology and the Academics

An Essay on Universities and the Scientific Revolution. By Sir Eric Ashby. Pp. vii+118. (London: Macmillan and Co., Ltd.; New York: St. Martin's Press, Inc., 1958.) 15*s*. net.

THE substance of this book is the series of Ballard-Matthews Lectures which Sir Eric Ashby gave in the University College of North Wales at the beginning of this year. It is a fascinating book and a timely one. It is also a courageous book. The problems raised are set in a wide background and put forward in a way which must appeal to a far wider public than those who are more immediately concerned with their solution.

The writer's thesis is the split personality which exists in British universities to-day. He outlines the four functions which the universities are attempting to fulfil: their functions to train people for the professions, to act as a nursery for gentlemen, statesmen and administrators, to provide a centre for scholarship and research, and to serve as a staff college for technological experts and specialists. It is startling and, at the same time, refreshing to find an analysis of the functions of a university in such simple and down-to-earth terms. The problem is to reconcile these four different functions in one and the same institution. As one would expect, the writer draws frequently on biological analogy. "In social institutions as in living organisms form and function are inextricably bound together. If function changes then form must adapt itself or the organism—and the institution—will perish." Adaptation in the universities is, it is maintained, by no means complete, and form is not everywhere fitted to function.

The first three chapters of the book are devoted mainly to a description of the reasons why, and the manner in which, technology became a university function in Great Britain. There is an absorbing first chapter on the development of science in the continent of Europe, the reasons for lack of enthusiasm at that time in British universities (that is, Oxford, Cambridge and the Scottish universities) for scientific thought, though British scientists individually played a notable part in the development of science in the eighteenth and early nineteenth centuries. He traces the early developments in France, "the mother of organized research", the export of science across the Rhine but not across the Channel and then the development of the German universities and Technische Hochschulen. The second chapter is devoted to the much later development in Great Britain, the influences which brought about the changes in Oxford and Cambridge and the growth of university colleges. There are some stimulating, and perhaps controversial, thoughts on the results of the impact of science on the universities, their impetus to the growth of intellectual freedom, the democratization of the academic world, and the growth of a cosmopolitan and even international spirit in the universities. Ashby then comes to their adoption of technology and shows how the differences in our environment led not to a facsimile of the continental institutions but to something very different and probably more fundamentally sound. The reasons for the development of technology within university precincts, rather than in separate institutions, are of particular interest to-day when efforts are being made on the Continent and in the United States to broaden and strengthen technology by bringing it into closer contact, both for staff and students, with the pure science and the humanities, to the mutual benefit of all three.

The symptoms of schizophrenia are the basis of the concluding chapters and the diagnosis is an able one. Finally, one cannot but refer to the delight of reading a book of such fundamental importance which is written in so engaging a way; its literary style, as one expects from Sir Eric Ashby, is impeccable. While there is an exceptional awareness of what has gone on and is going on both in Great Britain and overseas, there is a complete absence of that ostentation which too often accompanies so great a wealth of knowledge.

TECHNIQUES IN SOCIOLOGY

Survey Methods in Social Investigation

By C. A. Moser. (Heinemann Books on Sociology.) Pp. xiii+352. (London: William Heinemann, Ltd., 1958.) 35*s*. net.

IT is made plain in the introductory chapter of this book that the techniques with which it deals are more relevant to 'extensive' rather than 'intensive' inquiries; that is to say, it is primarily concerned with official surveys of the kind conducted by the Central Office of Information, market and opinion research, and the large-scale operations of social scientists. This is also evident from the fact that approximately a third of the book is devoted to the application of sampling methods, and a discussion of the problems that arise in the use of samples.

Although the book must, therefore, be regarded as restricted in its scope, despite its title, the introductory section also contains a discussion of the general nature of social surveys; it also ends with a broader treatment of methods of collecting information, including the use of documents, questionnaires, and interviewing, and a discussion of the methods of processing the data so obtained.

So far as the nature of social surveys is concerned, Mr. Moser points out very wisely that fact-collecting is no substitute for serious thought, remarking that "it is the ill-considered launching of surveys, leading to the waste of much time and money and the accumulation (often) of unwanted data, that has given rise to the scepticism with which some sociologists regard 'door-knocking' research." "It is no good," he adds, "blindly to apply the formal standardized methods generally used in official or market research enquiries, to many of the more complex problems in which sociologists are interested." This is all too true, but the comment would have been all the more valuable if it had been based on actual examples, of which there are many. Sociologists must be helped to learn from their mistakes, painful as the experience may be.

The main section of the book on sampling methods provides a useful text on which those actively engaged on large-scale inquiries can rely. So far as the collection of the raw data is concerned, on the accuracy of which the value of every survey is ultimately dependent, Mr. Moser is entirely correct in saying that problems arise which are different in kind, rather than in degree, from those arising out of sampling. This is an obvious point. Much more

attention should be directed to it rather than, for example, to the more elementary processes of sampling which are apt to be explained and discussed *ad nauseam*.

As Mr. Moser puts it, "our knowledge of data collection is, by comparison, primitive . . . One part of the survey process is tackled by a tool of high precision that makes accurate estimates of errors possible, while in the other parts errors of generally unknown proportions subsist". The impression is thus given that the high degree of accuracy with which the results of large-scale surveys are frequently stated may be misleading, perhaps very misleading indeed. This is probably true. Much more research into this difficult problem is required.

T. S. Simey

PLANTS OF THE FARM

Agricultural Botany

By Dr. N. T. Gill and K. C. Vear. Pp. viii+636. (London: Gerald Duckworth and Co., Ltd., 1958.) 63*s*. net.

ALTHOUGH botany began as the collection of information about economic and medicinal plants, the modern teaching subject of agricultural botany emerged as an eclectic version of 'pure' botany, based on economic examples. This was the plan of the late Prof. Percival's well-known textbook, even up to its last edition in 1936. Since the turn of the century, however, several fields of endeavour have developed a structure and outlook of their own. Thus, plant pathology and plant breeding are to-day largely independent disciplines, recognizably distinct in their methods of thought and action from mycology or genetics. Comparable trends are evident in crop physiology. The subject as a whole seems to be developing a coherent unity along lines indicated in part by Vavilov, and based upon the ecological connexions between its parts. This may well lead agricultural botany to a relationship to pure botany not unlike that of engineering to physics.

Against this background the present work is distinctly disappointing. It consists of a reasonably detailed and well-illustrated conspectus, on a taxonomic basis, of the agricultural and horticultural plants and weeds of temperate regions, with some tropical crop species added (400 pages), sandwiched between very much less satisfactory and far less well-illustrated accounts of plant breeding and plant diseases (about 100 pages each). Its stated aim is to meet the requirements of agricultural diploma and pass-degree students; but it would seem that many of them will find the systematic part more than adequate for their needs, while remaining unsatisfied by the remainder.

More serious than this lack of balance is the almost complete absence of any account of the extensive modern work on the physiology and ecology of crops and weeds. Yield is usually the most important characteristic of economic plants. The analysis of plant growth and yield is consequently an essential part of the contribution botany can make to farming; indeed, it can be thought of as the theoretical basis of agriculture. Yet the outstanding advances of the past thirty years in the study of the crop as an assemblage of growing and competing plants, continuously influenced by varying environmental factors, is not reflected in these pages.

The principal merit of the book, then, lies in the systematic description of agricultural plants, which fills a need by bringing together a useful body of fairly up-to-date information not elsewhere available in one volume. For this the work may be recommended, though the price may seem unduly high to some.

A. H. Bunting

". . . THE EAST WIND BROUGHT THE LOCUSTS"

Insect Migration

By Dr. C. B. Williams. (The New Naturalist: a Survey of British Natural History.) Pp. xiii+235+24 plates. (London: William Collins, Sons and Co., Ltd., 1958.) 30*s*. net.

AMONG British entomologists who have worked in the tropics within the past generation, there are probably not many for whom a visit to Rothamsted has not provided stimulation, together with an injunction from Dr. C. B. Williams to keep a look-out for butterfly migration. All who heeded his injunction, and all who know his comprehensive and critical book on this subject, published in 1930, will welcome this entertaining and copiously illustrated addition to the admirable "New Naturalist" series.

The present book, however, is perhaps one to arouse interest rather than to satisfy it. A serious reader, seeking to follow up some tantalizing allusion, and undaunted by an absence of references in the text, is still likely to be frustrated by the slim bibliography, with its sixteen titles since 1942, out of the several hundred of which Dr. Williams tells him—and makes use. Moreover, in the introduction the author makes a distinction between deliberate migration and drift on the wind, and he defines migration as "a continued movement in a more or less definite direction, in which both movement and direction are under the control of the animal concerned". But he does not say a great deal about the extent to which the material he presents satisfies his own definition: some species appear to be described as migrants mainly because they are often seen a long way outside their breeding areas—without much consideration of any contribution which may be made to these geographical displacements by the winds at the time.

Dr. Williams's editors suggest that his book may almost be regarded as a world detective story; and he tells how, for locusts, the original case for deliberate long-range migration appears to have collapsed under the evidence of synoptic meteorology. But in this book his own approach sometimes suggests the compiler of criminological statistics rather than the detective. Thus, eleven pages of tables, and four figures, demonstrate that a number of species of butterflies and moths have been recorded in Britain more frequently in some years than in others; but there is little examination of any possibility of an association of environmental conditions with such occurrences and their fluctuations—which is the more disappointing in view of Dr. Williams's own pioneer work on the effects of weather on insect populations.

But his readers, like the followers of the best detectives, will look forward to meeting him again

as he deals with new evidence. Urquhart has reported flights of up to 2,000 miles by individual marked Monarch butterflies in North America: details of such flights, which are still awaited, and of the wind-systems encountered during them, may perhaps provide the first rigorous demonstration of long-range insect migration in the strict sense of Dr. Williams's definition.

R. C. Rainey

HYDROGEN ION CONCENTRATION AND ACTIVITY

A Dictionary of *p*H Applications

By R. S. Evans. Pp. viii+78+xviii. (London: The Herbert Publishing Company, Ltd., 1957.) 10*s*. 6*d*. net.

The Book of *p*H

A simple and complete Description of the Theory and the Practice of the Measurement of *p*H as applied to Science and Industry. By R. B. Webber. Pp. 111. (London: George Newnes, Ltd., 1957.) 30*s*. net.

THAT two books on the applications of *p*H to industrial processes should appear together is a remarkable coincidence. Mr. R. S. Evans's book is sponsored by W. G. Pye and Co., Ltd., of Cambridge, and Mr. R. B. Webber's by Tintometer, Ltd., of Salisbury. Both books are designed to impress the industrialist, who, incidentally, is assumed to have no chemical knowledge, of the great importance that *p*H data may be to him and yet how very simple it is to make *p*H measurements. In the first, it is stated that glass-electrode *p*H meters are rapidly replacing colorimetric methods, which are not even described, while in the second, colorimetric and electrometric methods are very simply discussed, but it is emphasized that colorimetric methods are very much easier to operate, especially if use is made of the Lovibond comparator and Nessleriser in conjunction with permanent colour standards (of glass) which correspond with the colours of indicators at specified *p*H values, and which are mounted in a rotating disk to facilitate comparison. To estimate the *p*H of unbuffered, or poorly buffered, solutions, when it is essential to use as low a concentration of indicator as possible, the Nessleriser is used. In this method it is assumed that the effect of the *p*H of the indicator itself is rendered negligible. It would have been better if the isohydric indicator method had been given, but perhaps the reason for its omission is to be found in the assertion made on p. 81 that "the operators need not be particularly intelligent or skilful" to carry out colorimetric determinations.

Explaining the meaning of *p*H to the uninitiated is obviously something of a problem. Evans is content to leave the problem by saying that the *p*H value "may loosely be defined as a measure of acidity or alkalinity", whereas Webber starts off by stating that "the concept of *p*H is fundamentally very simple" and likens the *p*H scale to the centigrade scale of temperature, each number of the *p*H scale having "an exact meaning". Later, he declares that "the *p*H story is not an over-simple one". In the middle of the book he gives the mathematical expression which relates *p*H with hydrogen ion concentration, but towards the end he attempts to explain that it would be better to substitute activity for concentration. It must be comforting to the reader to be told that whichever view is accepted it will only make a difference in the observed *p*H value, within the *p*H range 2–12, of $\pm$ 0·02 *p*H unit.

Webber includes a couple of pages on measuring the hydrogen ion activity of non-aqueous solutions and refers to the cG scale which J. B. Conant introduced many years ago but which has not been seriously regarded. Such a discussion might be considered to be out of place in a book of this type.

Both volumes might be considered to have fulfilled a need, but that of Webber has done so more effectively.

H. T. S. Britton

APPLIED ACOUSTICS

Acoustics, Noise, and Buildings

By P. H. Parkin and H. R. Humphreys. Pp. 331. (London: Faber and Faber, Ltd., 1958.) 70*s*. net.

IN post-war Britain classical physics has been much neglected because of the great attractions of nuclear physics. Consequently, activity in Great Britain on the subject of acoustics is on a very small scale, although slightly more is now done than before the War, when the subject was practically ignored. In the United States and on the continent of Europe, on the other hand, much more work is done, and considerable effort goes into research and investigation. It is therefore not surprising that, although several text-books have been published in Europe or in America and some of the European books have been translated into English, the last important book was "Acoustics" by the late Alexander Wood, published in 1940. Messrs. Parkin and Humphreys are therefore to be congratulated on writing the present volume, which fills a long-felt want.

This book is not intended to be a text-book but a survey of the subject for those not qualified in physics, such as architects, engineers and others who may be interested in acquiring a reasonable knowledge. The first two chapters on the "Nature of Sound" and "The Behaviour of Sound in Rooms" are in elementary terms to act as an introduction to the subject. Chapter 3 describes "The Design of Rooms for Speech" and should be of great value to individuals interested in the improvement of the acoustics of theatres, lecture rooms, classrooms and similar buildings. Chapter 4 describes a much more specialized field, "The Design of Rooms for Music". The description of the various factors affecting design is very lucid, and most of the difficulties are described in considerable detail. Greater emphasis might, however, with advantage have been placed on the fact that the final criterion for such rooms is æsthetic and that personal opinion plays a large part in the final judgment. Chapter 5, "The Design of Studios", describes the design of studios for broadcasting, which is a very specialized field indeed.

Another feature of post-war civilization seems to be the absence of the orator capable of addressing a large audience without assistance from electro-acoustic devices. 'Public address' has consequently become firmly established even in quite small auditoria. Chapter 6, "The Design of High Quality Speech-Reinforcement Systems", is therefore a very valuable contribution and is particularly interesting for its description of the methods used for speech-

reinforcement in very large cathedrals such as St. Paul's and Salisbury. In such enormous buildings with very long reverberation times it has never been possible for the congregation to hear the service properly. In these circumstances, speech-reinforcement systems are the only solution. In the case of very large arenas, speech-reinforcement is also essential. It is to be hoped that the designers of speech-reinforcement installations, which up to the present have been extremely unsatisfactory except as an emulation of Donald Duck, may profit by the details given in this book.

Almost half the book, commencing at Chapter 7, is given up to the problems of noise, which is one of the most pressing problems in modern times. Chapter 7 describes various types of noise and their effects, while Chapter 8 gives a detailed description, in simple terms, of "Sound Insulation and Noise Control Practice" in all types of building. The details of "Sound Measurement and Calculation" are given in Chapter 9. Chapter 10 provides details of "Criteria for Sound Insulation and Noise Control", which is a very useful summary of the present position.

This book is well written and should prove of great value as a general survey of the subject. In several places where differences of opinion are known to exist, the authors might with advantage have indicated the regions of controversy. This is particularly noticeable in the chapter on "Sound Measurement and Calculation", some parts of which are the subject of argument at international conferences. The value of the book might perhaps have been increased, without appreciable increase of effort on the part of the authors, by providing references to the considerable literature in this field, since this would make it easy for an interested reader to follow up any particular problem on which he requires more information.

T. SOMERVILLE

THEORY AND APPLICATION OF INTEGRAL EQUATIONS

Integral Equations

By Prof. F. G. Tricomi. (Pure and Applied Mathematics: a Series of Texts and Monographs, Vol. 5.) Pp. viii+238. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1957.) 7 dollars.

Integral Equations and their Applications to Certain Problems in Mechanics, Mathematical Physics and Technology

By S. G. Mikhlin. Translated from the Russian by A. H. Armstrong. (International Series of Monographs on Pure and Applied Mathematics, Vol. 4.) Pp. xii+338. (London and New York: Pergamon Press, 1957.) 80*s*. net.

THE systematic study of integral equations was stimulated about 1900 by the somewhat sensational work of Fredholm in providing a proof of Dirichlet's principle asserting the existence of a solution of Laplace's equation under given boundary conditions. The wealth of ideas in Volterra's pioneer work began to be appreciated; and by 1908 or so the main lines of the classical theory had been laid down, with major contributions from Hilbert and Schmidt. The linear Fredholm and Volterra equation involves a term of the type:

$$\int K(x,y)\,\varphi\,(y)\,dy$$

where integration is over a constant range in the Fredholm equation, and from 0 to x in the Volterra equation, φ is the unknown, and K is a given function, the kernel. The method of successive approximation can be used to obtain formal solutions, as infinite power series in a parameter λ; but in the Fredholm case, the series does not necessarily converge for all λ, and Fredholm's great contribution was to replace the series by the quotient of two integral functions of λ. When the kernel is symmetric, $K(x,y) = K(y,x)$, connexion with orthogonal systems of functions is almost immediate, and leads to the Hilbert–Schmidt theory. If the kernel is of the form $H(x,y)/(x-y)^a$, so that the integral must be defined as a 'principal value', the equation is said to be singular, as are many of the equations which turn up naturally in applications, and we owe to Carleman the origins of two methods of coping with such equations. Non-linear equations have also come recently into prominence again, though Schmidt began their investigation some fifty years ago.

All this theory is set out beautifully by Tricomi, in a most readable book. The material is deliberately restricted to the classical theory, but there are numerous references to guide the reader to further work on the theory and to the wide field of recent applications. Great care has been taken with the presentation; the reader will require only a sound knowledge of elementary analysis. An acquaintance with the Lebesgue integral is desirable, since the main conditions on the kernel is simply that the two-variable integral of $|K|^2$ shall be bounded, but even this knowledge is not absolutely essential. Of introductions in English, French or German, this seems to me the most attractive.

Linguistic difficulties have not entirely concealed the fact that in recent years great progress in the application of integral equations to physical problems has been made by Russian mathematicians, particularly by those centred at Tiflis. Two recent translations of books by Muskhelishvili, on elasticity and on singular integral equations, have helped to make this work accessible, and now this translation of the second edition of Mikhlin's book has added to our knowledge. It is in two parts: the first 130 pages cover much the same ground as does Tricomi's book, more concisely and with slightly more demands on the reader. The remaining 200 pages are devoted to applications, starting from the basic Dirichlet principle, and concerned chiefly with elasticity, hydrodynamics and aerodynamics. Here, of course, it is necessary that the reader should have a sound knowledge of the fundamental principles of these topics, such as a good honours degree student should possess. The problems are culled from a wide field, but are mainly one-dimensional or two-dimensional; the author remarks that the accusation of ineffectiveness sometimes levelled at integral equations is not without justification when problems in three dimensions are involved; here, no doubt, is a field for further research.

This systematic exploitation of a powerful method is most welcome. The translation reads smoothly almost everywhere; but there are some references in the text (for example, pp. 234 and 264) to items which do not appear in the bibliography.

T. A. A. BROADBENT

UNESCO HOUSE, PARIS

ON the architects of to-day rests the responsibility of designing the heritage of to-morrow. But few architects in any era can have faced a task so onerous as the planning of the Unesco headquarters in Paris—an edifice that at one and the same time had to embody the spirit of modernism inherent in the United Nations Educational, Scientific and Cultural Organization, provide a functional base for its activities and blend with neighbouring buildings that had already spanned the centuries. That this has been accomplished is due to three internationally eminent architects, Marcel Breuer (United States), Pier Nervi (Italy), and Bernard Zehrfuss (France), who prepared the original plans, and a consultative panel consisting of Lucio Costa (Brazil), Walter Gropius (United States), Charles Le Corbusier (France), Sven Markelius (Sweden), and Ernesto Rogers (Italy), who approved them. Eero Saarinen (United States) also acted in an advisory capacity, and Eugene Callison (United States) supervised the building operations.

The Unesco headquarters, which was formally opened on November 3, is made up of three buildings. The most dominating of these is the Y-shaped seven-storied secretariat on the Place de Fontenoy. Viewed from the Eiffel Tower—which in its time had to pass through periods of acute criticism, ardent admiration and strong dislike before being accepted as a landmark of the great city—the frontage of the secretariat completes a semi-circle with a French ministerial building and combines to provide an effective background for the eighteenth-century Ecole Militaire.

Though it complements the surroundings so beautifully, the new building is still strikingly modern. Mounted on up-thrusting *pilotis* which give an even greater impression of height than its actual 94 ft., it bears the same relationship to its brick and stone companions as a jet airliner has to its bi-plane predecessors.

Six hundred offices are accommodated in the building, spreading out from the central point of the Y. While, on the exterior, the windows, numbering more than a thousand with a glass area of some 72,981 sq. ft., give the building a shimmering appearance, in the rooms the light is equally distributed with a clarity that reduces the need for artificial lighting to a minimum even on the dullest days.

The conference building, which is connected with the secretariat by an impressive hallway, owes its main impact to its fluted concrete walls and 'butterfly' roof covered in copper. Here in a deceptively small area (35,327 sq. ft.) are housed the main conference halls and committee rooms, including the Plenary Hall with accommodation for almost a thousand people, a Main Commission Room with 270 seats at tables for delegates and observers and 77 seats for the public, an Executive Board Room which can also be used by one of the large commissions and five smaller committee rooms with seating accommodation

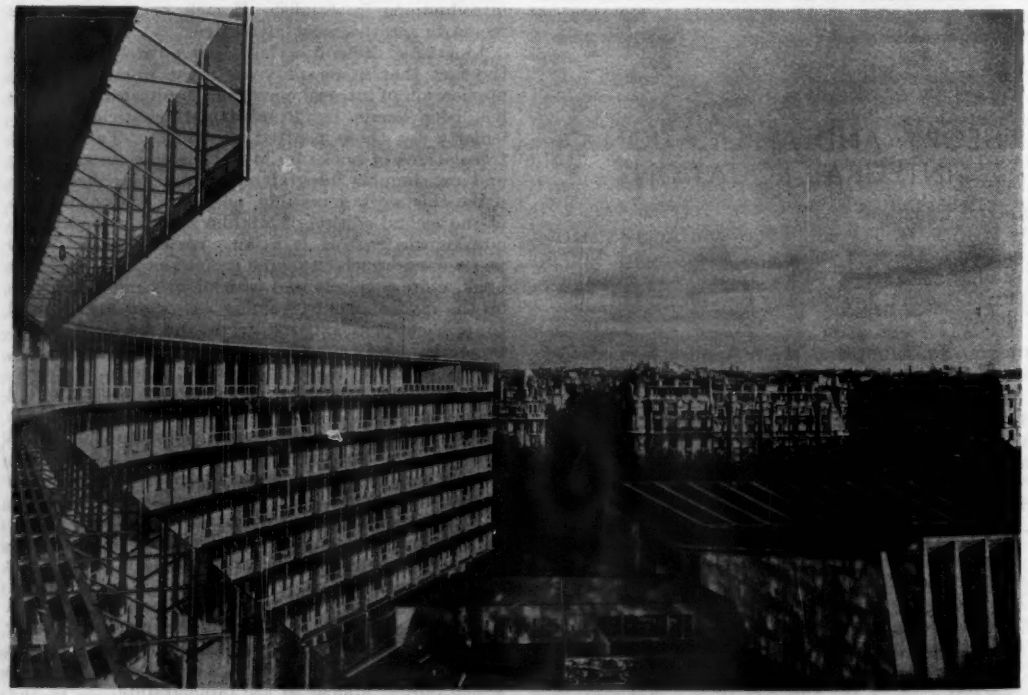

Fig. 1. Unesco House, Paris. Façade in Avenue Suffren *Photo: Unesco–Berretty*

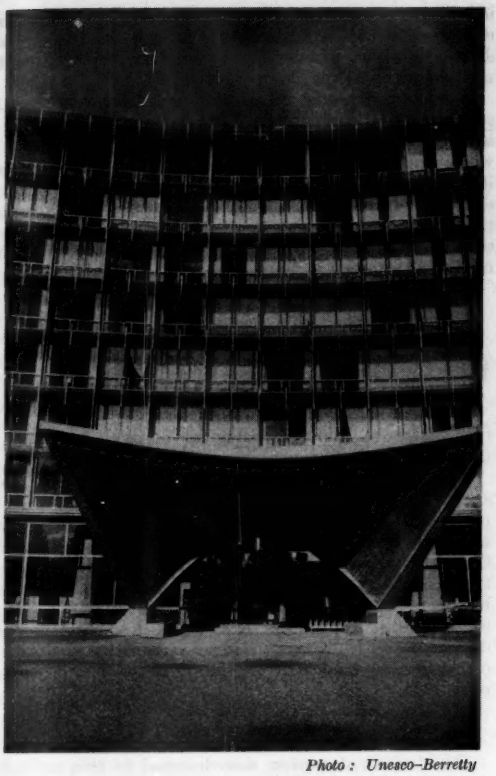

Photo : Unesco–Berretty

Fig. 2. Unesco House. Entrance from Avenue Suffren

ranging from 25 to 45. A special hall for international non-governmental organizations has also been provided along with ten offices and a Press room.

The permanent delegations to Unesco have been given offices in the third building, which follows the same exterior design as the secretariat building.

That these buildings should be constructed of the most modern—and cheapest—building material, namely, reinforced concrete, was not purely a budgetary decision. The limitation of funds (the ceiling was 9,010,000 dollars financed by interest-free loans from the French Government) imposed a certain degree of economy, but at the same time it was felt that the plasticity of concrete would give the desired freedom of architectural form and also be in keeping with the Organization's desire for functional simplicity.

The result is a pleasant contrast achieved by the juxtaposition of rough-surfaced concrete with Roman travertine and Brittany granite, the tone values being heightened by judicious use of wood for the window casings and other strappings. Great imagination has been used in the exploitation of the decorative worth of these construction materials, and even the concrete *pilotis* completely unadorned in themselves have a grace and force reminiscent of the pillars of ancient Greek temples.

But it is in the conference building that the extreme versatility of concrete is seen to best advantage. Here the fluting of the walls—fold after fold in wide corrugations—which adds so greatly to the æsthetic appearance, also has the practical result of ensuring perfect acoustics for the conference chambers. Similar unusual effects have been obtained by a fire staircase of pre-fabricated concrete blocks that winds its way in a spiral up one of the wings and by the canopy composed of two curved concrete surfaces that gives a dramatic quality to the doorway facing Avenue Suffren (Fig. 2).

An important part in making the headquarters what they are to-day is due to the Member States of Unesco. Engineers, furniture designers, electricians, office specialists, sound technicians, and industrial experts from ten countries have given an aura of internationalism to the most utilitarian objects, and in fulfilment of contracts workmen and equipment have come from Belgium, Czechoslovakia, the Federal Republic of Germany, France, Italy, Norway, the Netherlands, Switzerland, the United Kingdom and the United States.

In addition, thirteen countries undertook to present decorations and fittings for various parts of the buildings. Five of them, Denmark, France, the Federal Republic of Germany, Italy and Switzerland furnished committee rooms each demonstrating artistic trends in their own countries. The modern decor of the executive board room was a gift of the International Council of the Museum of Modern Art of New York made on behalf of the Government and people of the United States. The hall for the international non-governmental organizations was furnished by Czechoslovakia and the Press Room and Library by the Netherlands and Sweden respectively. The offices of the chairman and secretariat of the executive board are a gift of the United Kingdom and the office of the Director General is contributed by Belgium. The equipment and furnishings for the reception office, lobbies and gift-shop have been provided by Canada, Finland and Norway.

From the time the first line was drawn on the draughtsman's board it was recognized that contemporary art should be represented in these buildings. It was also realized that its selection would present considerable difficulties. So an advisory panel of art authorities, supplemented by members of the Architects Committee, was appointed to suggest appropriate artists. The panel consisted of H.E. Mr. C. Parra Perez (Venezuela), Mr. Georges Salles (France), Mr. Shahid Suhrawardy (Pakistan), and Sir Herbert Read (United Kingdom). With an allocation of 191,000 dollars, which had to cover artists'

Photo : Unesco–Pablo Volta

Fig. 3. Painting by Appel on the restaurant wall (2·8 m. × 4·2 m.)

fees, materials, the installation of contributions from Member States, etc., they commissioned the following works of art: Paintings by Afro (Italy), Appel (Netherlands; Fig. 3), Matta (Chile), and a photographic panel by Brassai (France) for the lounge, restaurant and cafeteria of the seventh floor; a mural by Picasso (Spain) for the wall in the delegates' hall and a fresco by Tamayo (Mexico) for the commission room; a bronze haut relief by Arp (France) for the outside Library wall and for the grounds an eye-catching mobile by Calder (United States), a massive travertine figure by Moore (United Kingdom) and two ceramics designed by Miro and executed in co-operation with Artigas (Spain). Noguchi was entrusted with the task of designing a garden in the Japanese style, for which the Japanese Government sent stones and plants.

No attempt has been made to build a monumental pile dedicated to posterity. This is a strictly utilitarian setting for a working organization, and Unesco, while appreciating to the full the practical facilities it offers, still takes greater pride in being party to the establishment of a school, no matter how small, the opening of a library or the equipping of a laboratory in pursuance of its main aim of peace through universal understanding.

HEALTH AND SAFETY IN THE FIELD OF NUCLEAR ENERGY

THAT the development of atomic energy involves important contributions from a wide range of disciplines is generally accepted. This is true also in respect of the more limited field of the health and safety aspects and was well illustrated in the second United Nations International Conference on the Peaceful Uses of Atomic Energy held in Geneva in September, where some 170 papers were contributed on subjects either directly concerned with, or closely relevant to, the problems of radiation safety. The time available, however, allowed only a small number of these papers to be read and discussed. The progress in biology has been reported in a previous article (see *Nature*, October 25, p. 1118), and, although reports continue to be received of reversible biological response for exceedingly small doses of ionizing radiation, the evidence at Geneva tended to support the basic levels currently adopted for permissible occupational exposure.

Control of Occupational Exposure

Several important papers gave factual information concerning the doses experienced in the atomic energy work in a number of countries having large or small atomic energy projects. One paper, from Canada, showed that the recent reduction in the permissible mean annual dose from 15 r. per annum to 5 r. per annum had been fairly successfully followed in the occupational exposures incurred. Some of the papers, such as one from Great Britain, reported not only external radiation doses but also the control of internally assimilated isotopes, air and surface contamination, urine data, and the instances where contaminated wounds had been dealt with. Another paper of considerable interest summarized experience of radiation exposure in a number of industrial factories, the work of which involved exposure to ionizing radiation; it was emphasized that in most instances radiation protection in such factories has to be achieved with far fewer protection personnel than is considered necessary in atomic energy plants. A further important paper from Canada described recent experiences in the protection of health in uranium mining. Ever since pre-war days, when a high incidence of occupational bronchial carcinoma was observed as a result of long periods of work in certain uranium mines, the subject of the protection of uranium miners has been of considerable concern. The Canadian paper indicated how the very real difficulties of good radiological control have been met in Canadian mines.

A further aspect of operational experience was shown by many papers dealing with the design of plant and equipment for safety, and an excellent example was a description in an American paper of the extraordinarily complex installation utilized for the processing of high-activity alpha-active materials in chemical and metallurgical procedures. Such installations represent heavy capital investment devoted essentially to providing virtually a guarantee of radiation safety in handling these highly toxic materials.

Control of Environmental Hazards

One technical session was devoted to this subject, on which fifty-seven papers had been contributed. The papers included a comprehensive review of the control of environmental hazard around the Hanford Plant in the United States, and also a paper from Great Britain giving the detailed radioactivity measurements on biological materials in the environment, such as milk, herbage and crops, following the nuclear reactor accident at Windscale in October 1957. (A brief synopsis of the Windscale data was presented in articles in *Nature* of September 6, p. 627.) In this session also a few papers dealt with the important subject of the fate of radioactive materials in soils and the transport through the soil – plant – animal food-chain. Other papers on this subject appeared in a further session on the uses of radioisotopes in agriculture. Problems of the discharge of liquid wastes were also covered, and included a report from Great Britain on experience in discharging large-volume dilute wastes to coastal waters. A study by the U.S.S.R. of the rate of turn-over of water in deep-water ocean depressions showed that the previous estimates of the time taken for water in these depressions to exchange with surface waters had perhaps been over-estimated, and the Russian report, which covered many of the known ocean-deeps, concluded that the disposal of very large amounts of activity in such depressions would be likely to lead to hazard.

The World Meteorological Organization presented a survey showing the importance of meteorology to safety problems in atomic energy, not only in the obvious instances of a reactor accident involving airborne release but also under normal operating conditions. In various sessions of the Conference

there were also several other papers dealing in some detail with each of these aspects.

Radiation Measurement and Dosimetry

Many of the papers concerned with radiation measurement were devoted to the use of gamma spectrometry. From the varied applications of this technique in the control of radiation hazards it is clear that it represents a most important advance. The application of the gamma spectrometric method to the measurement of gamma-radioactivity and beta-radioactivity (by bremsstrahlung) in the human body is now well known, and several papers showed the great value and promise of this technique. A further important application described in a paper from the United States was the use of this technique to measure traces of plutonium contamination in skin wounds and, in certain circumstances, a sensitivity of 4×10^{-5} microcurie of plutonium was attainable. The method offers an immense advantage in that the plutonium can be detected readily at depths in the skin far greater than the range of alpha-particles. The usefulness of the scintillation counting of alpha-activity was shown to good effect in a paper by Prof. W. V. Mayneord from Great Britain reporting direct measurement of the radium and thorium activities occurring naturally in human bone ash.

Progress was also noticeable in the dosimetry of airborne radioactive dust and the decay products of thoron and radon, the monitoring of which has presented considerable difficulties in the past. A paper from the U.S.S.R. by Baranov reported a useful application for health purposes of the $(n,2n)$ activation of carbon with the production of carbon-11 as a means of measuring fast-neutron fluxes in the energy-range exceeding 20 MeV.

Reactor Safety

Two technical sessions were devoted to this topic, on which about twenty-five papers had been contributed; these indicated substantial progress in this important subject. At the first International Conference in 1955 we had a report of experiments on a simple uranium – water reactor which was tested to destruction by power surges. At the present Conference we had reports on the theoretical and experimental investigation of reactor transients in full-scale power reactors. The development of experimental methods in this subject is advancing, so that we shall no longer have to rely so heavily in the future on unsupported calculations concerning safety in reactor kinetics.

Another important aspect of reactor safety in which there seems to be considerable progress is in regard to containment. Apart from reports from Sweden and Norway on novel underground containment for reactors, there appears to be a trend towards very strong compact enclosures which can give a considerable degree of guaranteed containment, and containment designs involving protection against shock-waves and missiles arising from fast-reactor 'runaway' were described from the United States. Indeed, it seems that, when the technology of the design and of the statistical testing of reactor enclosures (possibly on the model scale) has advanced somewhat further, we may well be in a position to tolerate nuclear reactors in heavily populated areas.

Several papers were again concerned with the evaluation of the accidental release of radioactivity from a reactor, and, while for many of the radiological effects the acceptable levels under accident conditions are in reasonable agreement, there appears to be considerable disparity with regard to acceptable emergency exposure of the thyroid; levels of 1,500 and 2,000 rad were suggested in some of the papers, whereas in the accident at Windscale the limiting level of milk contamination actually used corresponds to a thyroid dose of about 10 rad.

Some of the most valuable discussions at Geneva took place in a number of informal sessions in which specialists from several countries were able to meet and have free discussion on some of the more important problems in their particular spheres. One of the great values of the informal sessions was that spontaneous discussion could take place without the necessity for questions to be written down and handed up to the chairman in advance of the discussion period. One such session was devoted to problems of reactor safety, and included, among the introductory talks, one by Academician A. P. Aleksandrov on "Reactor Safety in the U.S.S.R." It was notable that the Russians tended to rely on design of control systems and on remote location rather than on containment to achieve safety, whereas other countries considered provision of satisfactory containment a necessary feature.

A further important informal session was devoted to criticality safety, and included an informal report of experience in a criticality accident at Oak Ridge in June of this year. Although a few persons were exposed to heavy doses of neutron and gamma-radiation ranging up to about 400 rem, the exposures were not lethal. Descriptions of events like this are extremely important in providing lessons for safety in design and operation of criticality facilities and, indeed, of nuclear reactors in general.

The general impression gained from a study of the large number of papers presented on subjects related to health and safety was that substantial progress is being made on many aspects of this important subject. It is considered exceptionally valuable that several countries had thought fit to report frankly their experience on radiation exposure both in regard to workers in their plants and to the environmental hazards of their operations. It is to be hoped that more countries will provide this kind of data in the future. A second important conclusion is that the standard of safety achieved is very high. It seems that the emphasis which has been placed on health and safety in the past has borne fruit, especially in regard to the amount of money which it is now accepted must be devoted to securing an exceptionally high degree of safety in nuclear reactors and plants. A further satisfactory feature of the reports presented at the Conference was the great strides which have been made in the techniques of measurement of radiations, especially for the purpose of health control. On the sensitive subject of radioactive wastes, there appeared to be universal recognition of the principle that the safety of any procedure for the disposal of radioactive materials, whether as liquid effluent or as gaseous activity to the atmosphere (which in the case of the noble gases may be difficult to avoid), must be demonstrated by comprehensive monitoring by the operating agency. This is a principle which might well be extended in other industries.

W. G. MARLEY

GRAPHITIZATION AND PLASTIC DEFORMATION OF DIAMOND

By Dr. M. SEAL

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Department of Physics, University of Cambridge

IT is well known that diamond is at normal pressures the thermodynamically unstable form of carbon, and that diamonds heated to a sufficiently high temperature change into graphite. A study has been made of this change, and two important results have been obtained. These are, first, that the change occurs via an intermediate structure of carbon atoms, and secondly, that plastic deformation of diamond can occur at 1,800° C. under the stresses set up by an expanding nucleus of graphitization.

In this investigation two types of diamond specimen were used—a fine powder of 0–1μ particle size, and large single crystals of up to a few millimetres across. The specimens were placed in crucibles of hard pure graphite and were heated in a vacuum of about 10^{-4} mm. mercury in an electric resistance furnace to various temperatures for 15–30 min. The heating was carried out by Dr. D. A. Melford or by Mr. B. L. Mordike of this Laboratory, and I wish to thank these workers for their help.

Experiments with diamond powder gave the following results. Heating to 1,200° C. produced little change and only diamond could afterwards be detected by electron diffraction. Heating to 2,000° C. produced a complete transformation to graphite. For intermediate temperatures of about 1,600° C. both diamond and graphite could afterwards be detected, but electron diffraction patterns also showed spots which were not due to either diamond or graphite. These spots could be indexed for a cubic unit cell, $a = 12{\cdot}3$ A. It is thought that they are due to some sort of intermediate arrangement of carbon atoms, possibly a regular array of diamond-like and graphite-like regions. The existence of such an intermediate structure is of obvious importance to our understanding of the way in which the change occurs. Thus Nath[1] postulated that the puckered {111} planes of carbon atoms of the diamond lattice would become flattened at high temperatures giving the plane hexagonal networks characteristic of graphite: the lattice would also have to expand in a direction perpendicular to these planes to give crystals of graphite which should then be of the rhombohedral type. There is, however, no evidence from the diffraction patterns for an abnormally high percentage of rhombohedral graphite in graphitized diamond, and it is difficult to see how any but a hexagonal intermediate structure could occur in the process that Nath visualized. The occurrence of a cubic intermediate structure must mean that all four {111} planes of the diamond are equally favoured in change. A detailed description of the diffraction patterns which reveal the presence of this intermediate structure will be published elsewhere.

Examination of graphitized diamond powders by transmission electron microscopy using both bright and dark field techniques showed that the graphite forms as crystallites about 100 A. across. These crystallites are formed on or within the individual fragments of the diamond powder which appear to retain their coherence and shape even after the conversion to graphite is complete. The graphite crystallites do not vary significantly in size with temperature of graphitization over the range investigated (1,400–2,000° C.), but they are, of course, more numerous for the higher temperatures.

With large single crystals the sequence of changes described in Table 1 was observed visually after graphitization.

Table 1

Temperature of graphitization	Appearance
1,200° C.	Slight dulling of surface
1,400° C.	Definite grey colour
1,500° C.	Diamond appears dark grey but still translucent
1,800° C.	Diamond black, opaque and starting to break up
2,000° C.	Small black fragments

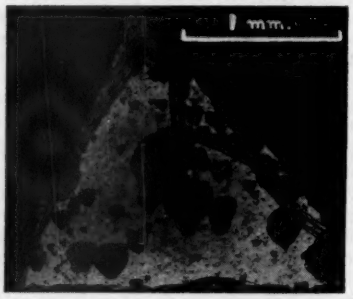


Fig. 1. Optical micrograph of a natural {111} diamond face after graphitization at 1,800° C.

Fig. 2. Optical micrograph of a feature produced on a polished {100} diamond face by heating to 1,800° C.

Fig. 3

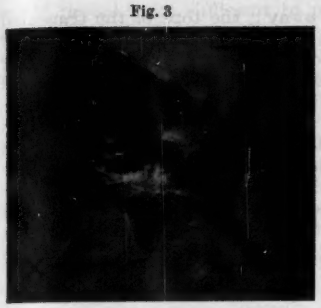
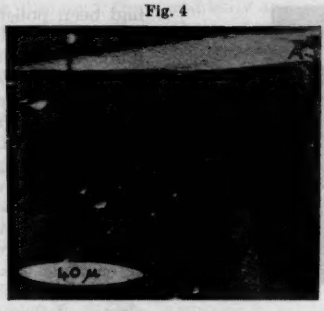


Fig. 4



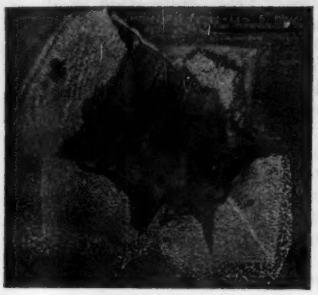


Fig. 6

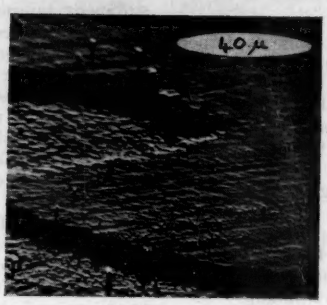


Fig. 5

Fig. 3. Phase-contrast optical micrograph of a large feature produced on a polished {100} diamond face by heating to 1,800° C.

Fig. 4. Reflexion electron micrograph of the limb *X* of the feature appearing in Fig. 3

Fig. 5. Reflexion electron micrograph of part of a {100} polished diamond surface after graphitization at 1,800° C. and abrasion with alumina. The surface graphite layer has been removed in places by the alumina

Fig. 6. Phase contrast optical micrograph of the feature of Fig. 3 after abrasion with alumina

These changes are similar to those described by previous workers[2,3]. Examination of the surfaces with an optical microscope showed no apparent change in the microstructure for graphitization at temperatures below 1,500° C. However, between 1,500° C. and the break up at about 1,800° C. marked changes in the surface topography did occur. Fourteen faces on eight diamonds graphitized at temperatures in this range have been examined. The features produced by the heat treatment on these faces were substantially similar, though at different stages of development. On three faces (two natural octahedral {111}, and one polished cube {100}), the features were particularly regular and well defined. These faces have been studied in detail, since they provide most information about the way in which graphitization occurs.

One of the natural octahedron faces is shown in Fig. 1: this had been graphitized at 1,800° C. The face is covered with dark patches which, though sometimes rather irregular in outline, do show a tendency to have a triangular shape. Examination at higher magnification revealed the presence of numerous similar but smaller triangular features. The surface relief was investigated using reflexion electron microscopy and it was shown that the triangles, etc., represent raised regions: the more regular of them are pyramidal in shape. The triangles are oriented with their sides parallel to the edges of the face, but they point in the opposite direction to the face. The polished cube face after graphitization at 1,800° C. showed similar features, but in this case they are square in outline and more regular in shape. An example is shown in Fig. 2. The features are again raised pyramids, and each has a central dark spot which represents a more sharply raised region. They have a wide variation in size, ranging from the limit of resolution of the optical microscope up to 0·3 mm. across for one particularly large composite feature (shown in Fig. 3). In each case where the height was measured it was found to be of the order of one tenth of the width of the feature. The squares are oriented, in some cases parallel to the crystallographic axes and in others at 45° to them. It can be seen that the large composite feature of Fig. 3 has three V-shaped limbs. These are portions of pyramids sloping upwards towards the irregular central region. Fig. 4 is a reflexion electron micrograph of one of these limbs (*X* of Fig. 3). The height of the point *A* above the general level of the surface is 4μ; the irregular central region is considerably higher.

The graphitized diamond on which the features shown in Figs. 2 to 4 appeared retained its original shape but became black and opaque after the heat treatment. It seemed likely that the graphite had formed as a surface layer (cf. Friedel and Ribaud[2]). To test whether or not this was so, the graphitized diamond was rubbed with a paste of water and fine alumina on a soft cloth. It was found that this treatment removed a surface film and that the underlying material was colourless and transparent—in fact, diamond. It was possible to estimate the thickness of the surface graphite layer in the following way. The abrasion with alumina removed the surface graphite layer in patches. The change in height at the edges of these patches was quite sharp, and it seemed that the abrasive had removed the surface layer by some sort of flaking process in which the entire thickness of the layer came away. A reflexion electron micrograph of a region at the edge of one of the patches is shown in Fig. 5. The thickness of the graphite layer could easily be measured from the length of the shadows cast by its edge. The abrasion grooves which were present on the original polished diamond surface before graphitization could also be seen after graphitization, both before and after the abrasion with alumina. Thus, the thickness of any layer removed from the top of the graphite layer by the abrasion with alumina was less than the depth of these grooves. For the film on the (100) surface which is being described, this was not more than 0·1μ. The remaining film, as seen in Fig. 5, was 0·5μ thick, and so the total original thickness of the graphite surface layer could be given as $0{\cdot}6 \pm 0{\cdot}1\mu$.

The effect of the abrasion with alumina on the large feature of Fig. 3 is shown in Fig. 6. The rougher regions where the surface graphite layer has been removed can be seen by comparison of Figs. 3 and 6. Examination of the surface by optical microscopy using illumination from behind showed that these rougher regions were transparent and that the central feature was opaque and spread slightly sideways

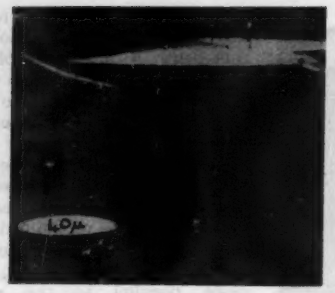
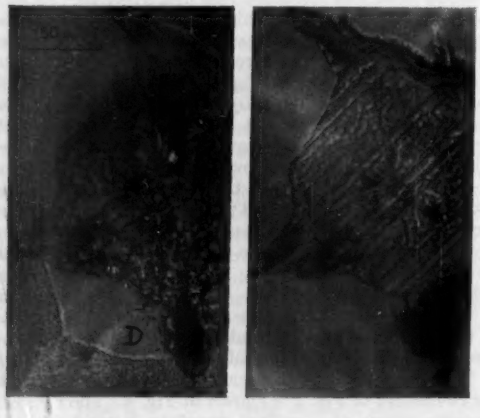


Fig. 7. Reflexion electron micrograph of the limb *Y* of Fig. 6

beneath the surface of the diamond. The V-shaped limbs were still present and could be seen to consist of transparent material. Reflexion electron microscopy (Fig. 7) and optical multiple-beam interferometry showed that they were still pyramidal in shape. The ridge of the limb *X* was found to have a slope of $2{\cdot}4° \pm 0{\cdot}1°$ and the point *A* to be $4{\cdot}2 \pm 0{\cdot}4\mu$ above the level of the original flat graphite surface (the level of the region *B* of Fig. 4). It follows that diamond has been transported to a position above the original level of the diamond surface. The only ways in which this can have happened are through plastic or elastic deformation of the diamond.

It does not seem to be possible to explain this transport of material in terms of elastic deformation of the diamond. The change in slope at the base of the pyramids is extremely sharp (Fig. 7), and it can easily be shown that the stresses necessary to produce so sudden a bending elastically would be impossibly big. One would, therefore, have to suppose that the stresses were relieved by cracking. This would have to be on such a scale that it should be readily visible. In fact, no evidence of such cracking could be observed even after the surface layers had been removed by polishing on an abrasive diamond wheel. Optical examination following this polishing did, however, give a confirmation of the nature of the feature. Fig. 8*a* was taken after the top of the feature had been polished away; the tops of the truncated pyramidal limbs (such as *D*) appear smooth and homogeneous in contrast to the rougher central region. Fig. 8*b* was taken after further polishing and represents a section of the feature a few microns below the original level of the surface: the region under the pyramidal limbs is indistinguishable from the surrounding diamond. It is concluded that the central region which is opaque and almost certainly graphite represents a nucleus of graphitization and that this, owing to the difference in densities, has expanded, forcing the surrounding diamond to deform plastically.



(*a*) (*b*)

Fig. 8. Phase-contrast optical micrographs of part of the feature of Fig. 6 after high-speed abrasion with diamond powder: (*a*) the top of the feature only has been removed; (*b*) abrasion has been continued and the surface seen here is a section through the feature a few microns below the original surface of the diamond

There is thus strong evidence which suggests that plastic deformation of diamond can occur at a sufficient temperature. This observation is of considerable interest since diamond is at normal temperatures a very brittle solid and all attempts to produce plastic deformation of it in the cold have met with at best doubtful success. There are, however, previous reports of plastic deformation being produced in this material at high temperature. Friedel and Ribaud[3] reported a relaxation of birefringence in a diamond heated to 1,880° C.: they interpreted this as indicating that plastic deformation had occurred. Evidence that plastic deformation can occur during the polishing of diamond was found by Seal and Menter[4]. Diamond is normally polished with diamond dust on a high-speed lap, and the conditions of abrasion are such that local frictional 'hot-spots' of 1,000° C. or more are almost certainly produced. Thus, high temperatures would again be involved in the plastic deformation. There is also evidence[5,6] that slip has occurred in some natural diamonds at some time during their geological history—very probably at high temperatures.

The particularly large feature which has been described was chosen for detailed study because of its size. The smaller features do, however, appear to be similar to it, and it is inferred that they are of the same nature. The experiments in which the surface layers of the diamond were polished away showed that these smaller features extend into the diamond to a depth comparable with their width in the surface. Thus, it is thought that all the raised square features seen on the {100} face and the triangular ones on the {111} faces represent nuclei of graphitization. These nuclei only occur near the surface of a diamond crystal and not within the bulk of the diamond.

The reason for this may perhaps be found from the following considerations. One may suppose that an incipient nucleus of graphite has formed within the bulk of a comparatively large mass of diamond. The nucleus originated in a smaller volume of diamond: it is therefore under compression from the surrounding diamond and occupies a smaller volume than it would otherwise have done. The diamond is in its turn under stress. The pressure within the nucleus can be calculated if simplifying assumptions are made. It is assumed that the nucleus is spherical, that it and the material surrounding it are both isotropic, and that the deformations are entirely elastic. The problem then becomes an elementary application of the laws of elasticity and the pressure is found to depend only on the compressibilities and densities of diamond and graphite and not on the radius of the nucleus. The numerical values of the compressibilities and densities at 1,800° C. are not known, but if the room-temperature values of these quantities are used then the pressure is found to be of the order of 10^5 atmospheres. Such a pressure

would probably be sufficient to make diamond the thermodynamically stable form of carbon. Thus the nucleation of graphite will not occur within the bulk of the diamond since the pressure produced in an incipient nucleus will be sufficient to inhibit the transformation. There is experimental evidence that pressures of the order of 10^4 atmospheres are sufficient to inhibit the transformation of diamond to graphite even though diamond is still thermodynamically unstable[7].

These considerations no longer apply, of course, at the surface of the diamond, and graphitization would be expected to proceed inwards from the surface, as is in fact observed. Moreover, an incipient nucleus just below the surface (forming perhaps at a dislocation or other fault in the diamond) might expand suddenly and burst through the thin shell of diamond above it. This is thought to be the explanation of the raised features which have been described. They are, as it were, miniature volcanoes which have burst through the surface of the hot diamond and forced it to deform plastically.

I wish to thank Dr. F. P. Bowden for his interest and advice, and Industrial Distributors (1946), Ltd., for a grant to the Laboratory.

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TYPHOON EFFECTS AT JALUIT ATOLL IN THE MARSHALL ISLANDS

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ON January 7, 1958, a small, very intense typhoon passed directly over Jaluit Atoll in the Marshall Islands (5½° N., 169½° E.). The first reports thereafter indicated that the typhoon had wrought many profound changes, especially in its effects upon the morphology of several of the islets and upon the vegetation and soils. Accordingly, the Pacific Science Board of the U.S. National Academy of Sciences, acting together with the Office of Naval Research and the U.S. Trust Territory of the Pacific, sponsored the formation of a party of seven scientists to conduct a brief, but intensive, field study at Jaluit. In addition to myself, the field party included Dr. A. H. Banner, director of the Marine Biological Laboratory, University of Hawaii; Dr. F. R. Fosberg, Pacific Vegetation Project, U.S. Geological Survey; Dr. J. Linsley Gressitt, chairman, Entomology Department, Bishop Museum; Dr. Edwin D. McKee, geologist, U.S. Geological Survey; Dr. Herold J. Wiens, professor of geography, Yale University; and Mr. J. B. Mackenzie, who has been director of the Agricultural Experiment Station maintained at Jaluit by the U.S. Trust Territory of the Pacific during the past several years. It is the purpose of this article to report very briefly and in a preliminary sense on the principal findings of this field party, which studied conditions on several different islets of Jaluit during April 24–May 2.

The Typhoon

Because of the paucity of weather observations over the ocean to eastward, the storm that struck Jaluit was not known to be of typhoon intensity before it struck. It was, however, being carried as a storm that had appeared at Palmyra Island (5° 53′ N., 162° 5′ W.) and was approaching Jaluit from the east. After striking Jaluit, the storm moved on a west-north-west heading through the Marshall and Caroline Islands and into the Philippine Sea, where it died out. Among the islands seriously afflicted by the storm were Ponape, Truk, and the Hall Islands, all in the Caroline Islands. When the typhoon intensity of the storm was first established it was named 'Ophelia'; and that name will be used here.

At Jaluit, judging from eye-witness accounts and from the field evidence, 'Ophelia' produced winds with sustained speeds of at least 125 knots and brought ahead of it and with it pronounced storm tides on which large wind waves were superimposed. Strong winds came initially from the north-east quadrant, then backed through west to south. There was at least one distinct lull, indicating that the eye of the storm crossed the atoll. There was initially a series of wave surges from the east, and these inundated several of the islets along the eastern reef, in one instance to a depth of 6 ft. above the ground in a locality that is more than 8 ft. above mean sea level. These first inundations occurred between late morning and mid-afternoon (180th meridian time) and were quite promptly followed by much lesser inundations upon the islets along the western rim, the wave having been renewed within the lagoon, which is about 15 miles wide (from east to west) and 30 miles long (from north-north-west to south-south-east). Later, in the afternoon or early evening, there was further, but only partial, inundation from waves moving eastward in the lagoon and waves moving south-eastward over the ocean to the west of the atoll. By dawn on January 8 the storm had subsided and the wind had become easterly, the normal trade-wind direction.

Geomorphic Changes

The observations of McKee and Wiens in particular, but also those of the other members of the party, led to the identification of several new geomorphic features, especially on those islets that suffered major

inundations. These include depositional and erosional forms.

The chief depositional forms produced by the storm were locally prominent gravel ridges upon the reef flat on the ocean side of some of the eastern islets; new or augmented beach ridges of gravel; gravel sheets, often tongue-shaped, extending across two-thirds of the islets in many places; and outwash features on the lagoon-side of the eastern islets. These lagoon-side sediments were strewn upon the reef and beyond into deeper water, as was shown by bottom samples obtained by Banner and McKee. They also may have helped form the gravel bars observed in some locations on the lagoon-side, both on the reef flat and beyond, though these bars also contain sediments derived from the floor of the open lagoon itself.

The most prominent erosion feature was the channels scoured out by the water. The best-developed ones originated at a break in the old beach ridge on the ocean-side of the eastern islets and extended several hundred yards across to the lagoon-side, where they gave rise to pronounced outwash features. Minor erosion features include plunge holes and scour pits.

Soils

On those eastern islets that were awash, the soils existing prior to the storm were either buried or scoured out over wide areas. On the islet of Mejatto, for example, more than half of the pre-existing soil now lies beneath a sheet of coral rubble that is from 5–6 in. to 2½ ft. thick. Severe scouring has sluiced off about one-fourth of the soil. The remaining 15–25 per cent is either partially eroded or else persists with little or no change, except, perhaps, in salinity.

A discovery made by McKee and Fosberg may prove to be of special interest. In a well cross-section, at a depth of about 3 ft., they found an undisturbed soil profile overlain by coral rubble to provide a disconformity that is precisely analogous to that produced by 'Ophelia'. This suggests that it might be possible to date, by the carbon-14 technique, those typhoons in past centuries that were sufficiently intense and sufficiently 'on target' to yield gravel sheets upon atolls anywhere.

Vegetation

The principal broad-scale effects of the storm upon the vegetation is well summed up by Fosberg in the introductory portion of his report (now in manuscript). His remarks should be viewed in the light of the fact that prior to the storm Jaluit was densely vegetated, since it lies in an area where the rainfall averages close to 200 in. a year.

"The effects of Typhoon 'Ophelia', even on the same vegetation type, or on the same plant, were by no means identical in all localities and parts of the atoll. In general, the islets on the eastside of the atoll suffered much more damage to their vegetation than those on north, south, and west. Also . . . narrow islets and parts of islets were far more affected than broad parts. This was well illustrated on Jaluit Islet, where the narrow parts south of Jabor were in places completely stripped of vegetation. . . .

"Many trees were uprooted. . . . Some were snapped off. Branches were broken or torn off of most of those that remained standing. Some exotic plants were killed or their above ground parts killed by salt. In places large scale burial of plants by gravel occurred. Elsewhere the soil with its vegetation was scoured away. Many tree trunks were seen in the lagoon on the shallower slopes along the east side. Masses of vegetable debris were strewn at random on the shallower slopes along the east side."

From the observations of Fosberg, Wiens and Blumenstock it is estimated that among those islets studied the greatest destruction was on Mejatto and northern Jaluit, both islets on the eastern reef, where 70–90 per cent of the trees were either completely uprooted or snapped off below the crown; while the least destruction was on western islets, where only 20–50 per cent were uprooted or snapped off. As for the comparative resistance of different tree species to the wind, Fosberg observes that *Pemphis*, *Cordia*, *Calophyllum*, *Casuarina* and *Bruguiera* "perhaps stood up best", while *Pandanus*, breadfruit and *Terminalia catappa* "perhaps fared worst".

Terrestrial Fauna

Gressitt observed that there was no evidence that the storm had eliminated any terrestrial faunal species. There were, however, pronounced effects upon populations and breeding-rates, with local extinction where vegetation was eliminated. He states: "Groups which seem to have suffered most appear to be rats, soil insects, grasshoppers, and scale insects. The birds (sea and shore birds, dove, cuckoo), lizards (geckos, skinks), brackish water shrimps, amphipods, land crabs, and spiders seem to have suffered very little. . . . *Culex* mosquitoes are breeding abundantly in cisterns which were inundated by sea water. House-flies and other filth flies are breeding abundantly, partly in privies as usual, and partly in some of the piles of accumulated decaying vegetation. Other insects found in the latter habitat, and under bark of dead trees, are breeding up large populations because of increase in their habitat as a result of the extensive killing and felling of trees and other plants. Still other insects, mainly moths and hemipterans, are breeding up large populations on new growth, apparently as a result of greater mortality among their parasites".

Submarine Features and Marine Life

Banner examined the submarine conditions within the lagoon by diving to depths of 30 ft. and more in many different places. He also examined depositional materials on newly formed bars and upon the islets, with special reference to its probable derivation. It was not possible, however, to observe the submarine features along the reef front in the surge channel zone because of heavy surf conditions.

On the bottom of the lagoon below low low-tide there was no evidence of disturbed conditions. Even delicate corals were not broken. In contrast, it seems likely that the outer reef front suffered pronounced changes, at least in some sections, because more than 75 per cent of the coral rubble forming the new ocean-side bar off Jaluit Islet is comprised of materials newly wrested from the outer reef.

The storm seems to have had no great effect upon the fish life in the lagoon. The inhabitants report better fishing since the storm than there was before; but it is possible that they gain this impression through having to fish more intensively than before, since vegetable food is in short supply.

Demography and Cultural Effects

Fourteen Marshallese died in the storm. Two more died of exhaustion immediately thereafter. This toll was surprisingly light considering the fact that there were some 1,200 inhabitants living on the atoll when the storm struck.

The low fatality-rate was the result of three factors. Imroj, the most densely populated islet, was not completely under water. Further, about 150 natives of Mejatto happened to be visiting Imroj for a social event when the storm waves swept their islet. And the natives on Jaluit Islet were able to take refuge in sturdy Japanese, cement-block buildings that were the only structures to withstand the storm.

On islets not under water, nearly all habitations were destroyed. Buildings made of board and corrugated iron blew apart. Native buildings, of grass, fibre and pandanus, blew down; but according to informants these were readily pushed back up, reinforced, and thus re-established after the storm.

Many of the inhabitants on the eastern, inundated islets have been forced to move to Imroj. Already, however, a few are beginning to move back home. Great quantities of supplementary food are being supplied by the U.S. Trust Territory Government, and these supplies will have to continue for a long time. Though replanting is taking place and though new vegetation is sprouting from vegetative debris, it will doubtless be at least a decade before the atoll has really recovered. Meanwhile, it is planned to re-study the atoll at intervals to learn how an atoll recovers from a typhoon strike.

FLUORINE COMPOUNDS

AT the recent meeting of the British Association in Glasgow, one of the sessions in Section *B* (Chemistry), on September 2, was devoted to various aspects of the chemistry of fluorine compounds. Dr. J. Craik presided during the first part of the meeting, and Prof. R. A. Raphael for the latter part.

The first paper, given by Dr. J. C. Tatlow (University of Birmingham) was entitled "Fluorocarbons: a New Branch of Organic Chemistry". As a result of investigations during the past twenty-five years, it is now apparent that there exists a new type of organic chemistry, based upon the carbon–fluorine system, and paralleling the carbon–hydrogen system of ordinary organic chemistry. Thus, analogous to the saturated hydrocarbons, there are the fluorocarbons. Many open-chain and alicyclic compounds of this type are now known, with up to thirty or more carbon atoms. Fluorine can form the basis for this new branch of organic chemistry because the bond between a carbon and a fluorine atom is an extremely stable one, and also because the size of a fluorine atom is not too great to allow saturated fluorocarbon chains [$CF_3.(CF_2)_n.CF_3$] to exist without strain. If the atoms were very much larger, there would be insufficient room for enough of them to be carried on a carbon skeleton. However, fluorine atoms are bigger than hydrogens, and in a fluorocarbon they shield the backbone of carbon atoms, and thereby protect them from attack by chemical reagents, much more effectively than is the case with hydrogen substituents in hydrocarbons. Thus, two factors contribute to the great stability of fluorocarbons which are among the most unreactive organic compounds known. They are non-inflammable and are resistant to attack by acids, alkalis, oxidizing agents, and reducing agents.

As in orthodox organic chemistry, a vast range of compounds based on this parent series is capable of existence, since various other atoms and functional groups can be substituted in the molecules. Such derivatives are rarely prepared from fluorocarbons themselves (because of the great stability mentioned above they will seldom take part in controlled reactions). However, very many classes of fluorocarbon derivatives containing a variety of functional groups can be made in other ways. Simple examples of types now freely available are fluorocarbon carboxylic acids (for example $CF_3.CO_2H$), sulphonic acids (for example, $CF_3.SO_3H$), alcohols (for example, $CF_3.CH_2OH$), and amines (for example, $CF_3.CH_2NH_2$; compounds containing the groups $—CF_2.OH$ and $—CF_2.NH_2$ are not known). In all cases a complete homologous series can be made. The fluorocarbon part of the molecule can modify considerably the properties usually conferred on an organic compound by the functional group. Thus, the acids $CF_3.CO_2H$ and $CF_3.SO_3H$ are very much stronger than their analogues containing CH_3-groups. Usually, however, the fluorocarbon residue retains its inertness to chemical attack. Hydrogen and the other halogens can accompany fluorine as substituents on a carbon skeleton, and again various functional groups can be present as well, so that vast numbers of fluorine compounds are potentially capable of existence.

Recently, routes to perfluoro–aromatic compounds such as hexafluorobenzene have been opened up, and this most interesting new section of fluorocarbon chemistry is being investigated actively at present.

Because of their general stability, organic fluorine compounds are becoming increasingly important industrially as specialist materials. One typical example is in chromium plating, where long-chain fluorocarbon sulphonic acids (for example, $C_{10}F_{21}.SO_3H$), which are surface-active, can be employed to reduce spray above the plating baths. These use hot chromic acid, which attacks and destroys hydrocarbon-based detergents.

Fluoro-polymers are finding ever increasing applications. Recently, a series of rubbers has been introduced which are very stable towards heat and chemical reagents.

Mr. H. R. Leech (Research Department, I.C.I. General Chemicals Division) spoke next on "The Industrial Advance of Fluorine". A generation ago, fluorine was an 'awkward' element. The compounds in which it occurred naturally were inert and insoluble, but when they were brought into chemical usage, great difficulty was experienced in handling hydrogen fluoride and the element itself. This situation has now been changed completely, however. It is not always realized that fluorides are quite widespread in Nature, the element being thirteenth

in order of abundance in the Earth's crust—more abundant than chlorine. Anhydrous hydrogen fluoride is now an important article of commerce and is made on a considerable scale from fluorspar and concentrated sulphuric acid. Handling it involves no great difficulties if the right equipment and techniques are used, and it may be transported in cylinders and tank cars. The same applies to fluorine itself.

One of the most important routes to organic fluorine compounds is by halogen exchange. The fluorine of hydrogen fluoride or a metallic fluoride is exchanged for another halogen in an organic structure. In this way, a range of simple fluoro-chloro-aliphatic compounds can be made. Compounds such as dichlorodifluoromethane have found wide application as refrigerants and as aerosol propellants. They are made in large quantities and are marketed under the trade names 'Freons', 'Arctons' and 'Isceons'. From compounds of this type, by simple reactions, the olefins tetrafluoroethylene and chlorotrifluoroethylene are obtained. These may be polymerized to give the fluoro-polymers, 'Teflon' or 'Fluon', and 'Kel-F', respectively. The first of these, particularly, has remarkable properties, being non-inflammable, and chemically stable. Also, it has valuable 'low friction' and 'non-stick' characteristics; one use arising from the last is for coating rollers which handle dough in bakeries. Polymers such as these are finding ever wider applications in many fields. Another valuable product of this halogen-exchange method of fluorination is the new non-inflammable anæsthetic 'Fluothane' ($CF_3.CHClBr$) recently made available by Imperial Chemical Industries.

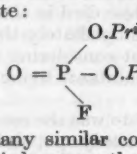
A second route to fluorine compounds is through the element itself. The preparation of fluorine by electrolysis of anhydrous hydrogen fluorine–potassium fluoride systems is now a routine operation and considerable quantities are used in the field of atomic energy. The preparations of chlorine trifluoride, sulphur hexafluoride, and uranium hexafluoride are carried out via elementary fluorine.

In the organic field, though much laboratory work has been done on fluorinations with the element itself, the reactions are difficult to apply on a larger scale and there has been little industrial development of this sort. The same is true of fluorinations involving high-valency transition metal fluorides such as cobaltic fluoride, though this is a valuable research method.

The electrochemical method of fluorination is potentially very useful, however. The organic compound to be fluorinated is dissolved in anhydrous hydrogen fluoride and electrolysed at voltages below those necessary for the liberation of free fluorine. Many functional groups are left intact in this process so that various types of fluorocarbon derivatives can be prepared in this way. Examples are fluorocarbon carboxylic acids, sulphonic acids, ethers and tertiary amines.

The development of the chemistry of fluorine is likely to see many further advances, and new kinds of compounds are constantly being made available and their potential value explored.

Dr. B. C. Saunders (University of Cambridge) presented a paper entitled "Physiological Properties of Toxic Organic Compounds containing Fluorine". He gave a most entertaining account, including some personal reminiscences of his own work. First, toxic fluorine compounds containing P—F linkages were described. Compounds of this type were first reported by Dr. Saunders and his colleagues in 1941. One of the most interesting was di-*iso*propyl-phosphorofluoridate:



and since then many similar compounds have been made. Tests carried out on the investigators themselves showed that exposure to low concentrations of the vapours of these compounds caused constriction of the pupil of the eye (myosis), powers of accommodation being affected and photophobia and intense headaches being experienced. Higher concentrations (tested on small animals) caused a quick knock-out action, the symptoms being muscular weakness, gasping, and finally cessation of respiration. The compounds are toxic by injection as well as by inhalation.

All these effects can be explained on the basis of interference with the enzyme cholinesterase, which is intimately concerned with the propagation of certain nerve impulses—hence the names nerve gases and anticholinesterases given to this class of compounds.

Dr. Saunders gave a brief account of the mammalian nervous system, and described how, when the acetylcholine liberated at the ends of the parasympathetic nerve fibres has performed its job by causing the appropriate physiological response, it is normally destroyed by being hydrolysed, by the enzyme cholinesterase, to choline and acetic acid. The nerve gas inhibits the action of cholinesterase and so allows acetylcholine to accumulate. This inhibition may be caused by the formation of a hydrogen bond between a hydrogen atom of the enzyme and a fluorine atom, followed by attachment of the phosphorus to a basic group of the enzyme.

These toxic compounds have found applications as 'systemic' insecticides which are absorbed by the plant and then transferred to other parts, so that any insects attacking the plant are killed. To be of use such compounds should be of negligible toxicity towards mammals and also should be broken down at such rates as to be entirely innocuous when the crops are harvested.

A second and most important group of toxic fluorine compounds is a series related to monofluoroacetic acid. Here, there is a C—F link, but with one such bond only in the molecule. These compounds are convulsant poisons. Comparable toxicities are shown by fluoroacetic acid, its salts, esters, and simple derivatives, whereas di- and tri-fluoroacetic acid and their derivatives are inactive. In general, most compounds that can be hydrolysed or oxidized in the animal body to fluoroacetic acid are toxic (fluoroethanol has properties identical with those of the acid). This applies also to derivatives of longer-chain ω-fluoroacids, $F(CH_2)_n.CO_2R$, where n is odd, though if n is even the compounds are non-toxic. It has long been thought that fatty acids are oxidized in the animal body by loss of two carbon atoms at a time, owing to oxidation at the carbon atom β to the original carboxyl group, and the toxic properties of the long-chain ω-fluorocarboxylic acids afford a striking proof of this theory. If the carbon skeleton of a toxic long-chain acid is modified so that β-oxidation cannot take place, the compound is devoid of toxic properties.

The reason for the toxicity of the compounds related to fluoroacetic acid is that they interfere in

the Krebs tricarboxylic acid cycle. The body does not distinguish between acetic acid and its derivative with one fluorine substituent in place of a hydrogen, and fluoroacetate is built up into fluorocitric acid, causing a jamming of the normal tricarboxylic acid cycle.

The South African plant gifblaar contains sodium fluoroacetate and is extremely poisonous. It seems to grow best where the water has a high fluorine content. The enzymes involved in this synthesis of fluoroacetate are not yet known.

Dr. Saunders concluded by speculating as to whether other living systems, for example, green algae or even the animal body, by some 'deranged' mechanism might possibly synthesize organic fluorine compounds from inorganic fluorides. Some of these might be deleterious (for example, fluoroacetate), some beneficial (*cf.* recent reports of potent synthetic fluorine-containing analogues of steroid hormones).

The last paper, "Fluorine and Dental Decay, Fifty Years of Research", was by Dr. J. Campbell (Glasgow Dental Hospital). He emphasized that dental decay is the most prevalent human disease and is increasing at a rate which outstrips the capacity of the dental profession to deal with it. Some possible preventive measures, for example, reducing the consumption of sugar, are impossible to apply because of lack of public support. Fluoridation of domestic water supplies, however, will reduce dental caries by 60 per cent and has been recommended by the World Health Organization. Regarding the speculation raised by Dr. Saunders, Dr. Campbell pointed out that fluorine is in all of us, anyway, and is a normal constituent of human teeth. Many natural water supplies contain fluoride ion in relatively large quantities, much more than would be introduced by fluoridation.

Fifty years ago dentists noticed that children in certain districts of the Rocky Mountains had mottled teeth but were considerably less susceptible than other children to dental decay. They suspected a constituent of the water, and later, fluoride ion was identified as the responsible agent. Subsequent work showed that a fluoride ion content of about 1 p.p.m. would give a considerable degree of immunity to dental decay without discolouring the teeth. Such discolouring occurred only if the concentration was considerably higher. Various examples of the effects on dental health of high and low concentrations of fluoride ion in natural waters in North America and in Britain were quoted, including the cases of the children from North and South Shields. During the wartime evacuations it was found that the teeth of the children from South Shields were better than those of the children from North Shields and it was shown that the water supply in South Shields contains the optimum concentration of fluoride ion while that of North Shields is deficient. The advantages of artificial fluoridation of the water supplies of towns where the fluoride content is deficient are thus apparent. Intensive investigations have shown that artificially fluoridated water is identical with water that has been fluoridated by Nature, and that no industrial or other processes would be harmed by the addition of such small traces of fluoride ion. Water engineers are able to guarantee the accuracy and the uniformity of the additions of fluoride ion. Artificial fluoridation was first started thirteen years ago in certain towns in the United States and Canada, and has been completely successful. Dental decay has dropped by some 60 per cent and general health standards have been maintained. Fluoridation is now widely practised in North America (some 34 million people there are now receiving fluoridated water). It was started about two years ago in Britain on a very limited scale. All the results so far have been in accordance with expectation.

In conclusion, Prof. Raphael said that the issue of whether or not the fluoridation of water supplies should be carried out must be judged on the scientific facts which are now well established.

J. C. TATLOW

THE GEOLOGISTS' ASSOCIATION

A CENTENARY

By PROF. DAVID WILLIAMS

Imperial College of Science and Technology, London

SINCE its inception in 1858, when a few ardent amateur geologists met at No. 2 Upper Wellington Street, Strand, London, "modestly to seek mutual help as learners", the Geologists' Association has attracted recruits from all walks of life, from the veriest tyro to the savant steeped in geological lore, until now its membership is 2,032. The Association was opportunely born at a time when geology had so captured the imagination of the layman that the original prospectus could rightly claim that "There is no branch of Science which attracts so general—it may be said so popular—an interest as Geology". Only six weeks after the founding of an Association had first been mooted, nearly two hundred enthusiasts heard an inaugural address on "The Finding of True Facts".

Among the original objects and aims of the Association were the reading and discussion of papers, the exhibition of specimens, the dissemination of geological knowledge by printed *Proceedings*, and the holding of excursions. All these laudable aims have remained inviolate, though none has achieved such paramount importance as the excursions or field-meetings. Indeed, the longevity and continued prosperity of the Association is due in large measure to the genial companionship and mutual encouragement of its amateur and professional members, engendered and nurtured among hills and dales, mountain crags and lowland plains. Characteristically, to mark its centenary year, the Association held a series of field-meetings, ranging from Land's End to John o' Groats, besides which a wide range of geological guide books is being issued dealing with classic areas, the coasts of Britain and the environs of university cities in Britain.

By 1908, the jubilee year of the Association, the membership had risen to 661, by 1925 the total had

reached 1,000, and in 1951 the 2,000 mark was passed for the first time. Candidates, irrespective of age or sex, have always been welcomed to membership, and many a novice has thus been inspired by the Association to become an eager disciple and exponent of geology. With few exceptions the present rules differ but slightly from those of a hundred years ago. The prospectus of 1858 stated that "the subscriptions have purposely, and with deliberate consideration, been fixed at a rate which will exclude none from the benefits it can give". Indeed, it is quite remarkable that not until 1952 was the Association compelled, by the fall in the value of money and the increased cost of publishing its *Proceedings*, to raise the annual subscription from 10*s*. to £1.

Unlike many other scientific societies, the Geologists' Association has never had a home or headquarters of its own ; thanks to the kindness and generosity of various bodies and institutions, however, it has always been able to hold regular monthly meetings for the presentation of papers and the delivery of lectures. During the first few years these were held at St. Martin's Hall, Long Acre, at the College of Dentists and at the Medical Society of London ; but from 1867 until 1939 the Association received spacious hospitality from University College, London, and since then it has enjoyed the privilege of meeting in the dignified rooms of its 'senior partner', the Geological Society of London.

In 1922, the Council sanctioned the formation of Local Groups, especially in areas where members were not within easy reach of ordinary meetings and field-meetings around London. The first to be formed was the North-East Lancashire Group in 1922 ; this was followed by the St Helen's District Group in 1929 (now defunct), the Midland Group in 1937, the North Staffordshire Group in 1949, and by the Jamaica Group in 1955. Incidentally, as part of the centennial celebrations, the Jamaica Group is erecting in the island, at Halse Hall, Kingston, a memorial plaque in honour of Sir Henry de la Beche, the first director of the Geological Survey of Great Britain, who lived there as a child and again in 1823–24.

In 1923, a Weald Research Committee was formed for the purpose of making a complete survey of the whole of the country involved in the anticlinal structure of the Weald ; it has published a long series of original papers and reports of field-meetings, numbering almost a hundred in all. For several years during the 1920's, a Temporary Sections Committee organized the collection of records of transient sections, such as road excavations and building foundations, in the metropolitan area, a task which has been successfully continued by the London Naturalists' Society.

The Association is indebted to many of its members, both past and present, for generous bequests, some of which exist in the form of special funds or awards—as the Foulerton Award Fund, the Henry Stopes Memorial Fund, and the G. W. Young Investigation Fund.

Papers submitted for reading at ordinary meetings have steadily increased in number, while their diversity and standard arouse widespread commendation in geological circles. The first annual conversazione appears to have been held in 1863 ; during the long sojourn at University College the conversaziones attracted large gatherings to the main library and in later years to the Great Hall. Following a war-time interruption from 1939 to 1941 this popular function, thereafter named the annual reunion, has been held early in November at various institutions, usually at the Chelsea Polytechnic. During the present century the attendance has seldom been less than 50, and has sometimes reached 350.

One-day excursions, which started in 1860 on quite a small scale, have been a constant and enjoyable feature of the Association's activities. The first two-day field-meeting was conducted in 1863, and since 1871 outings of two days or more have been customary—apart from war years—at Easter and Whitsun. Moreover, during the summer months, long excursions. lasting up to a fortnight, have been arranged in various parts of the British Isles and on more than twenty occasions to Continental countries, including Austria, Belgium, Czechoslovakia, France, Italy, Norway and Switzerland.

One of the original aims of the Association was the printing of *Proceedings*, separate memoirs and notice papers. Until 1911 the *Proceedings* appeared every two years, but since then they have been issued as annual volumes in four parts, with maps and illustrations. Among the host of published papers, covering most facets of geology, a goodly proportion has dealt with the geomorphology and stratigraphy of southern England. Many of them rank as classical contributions to the literature of geology. The publication in 1910 of the jubilee volume, "Geology in the Field", describing areas in England and Wales visited by the Association, marked a milestone in its history. Apart from two months each summer, it has long been the practice to issue monthly circulars announcing forthcoming lectures and field-meetings.

The Association's century of progress has been largely due to the selfless devotion of its officers, and of the directors and secretaries of field-meetings at home and abroad, all of whom have willingly served without monetary recompense. Since 1900, the pleasant custom—never a rule—of electing presidents alternately from among amateur and professional members has been maintained with but one exception. The arduous office of treasurer and the key-post of general secretary have usually been in the competent hands of amateur members, while most of the editors have been professional geologists, and the less conspicuous but important roles of librarian and secretary to the Publications Committee have been filled by a line of enthusiasts, many of whom have served for long periods.

In the future, as in the past, amateurs will continue to be the mainstay of the Association ; among their ranks there will always be some of international calibre, many will be active in the important task of assembling local details and recording ephemeral sections, and all will be attracted to the Association by a spirit of inquiry, by a stimulating out-door scientific pursuit with kindred souls, and by a love of Nature. Happy indeed is the Geologists' Association that it can look back with justifiable pride upon a hundred years of almost continuous expansion and progress, and forward in confident anticipation of still greater accomplishment.

Besides the launching of a series of guides, the centenary year is being commemorated by the publication of a volume entitled "The Geologists' Association 1858–1958", the delivery of several special lectures, the holding of a reunion on November 10 in the apartments of the Royal Society and the Geological Society, and a centenary year dinner on November 11 in the Connaught Rooms, London.

OBITUARIES

Prof. J. F. Joliot, For.Mem.R.S.

Le monde scientifique a été frappé par l'annonce de la mort de Jean Frédéric Joliot le 14 août à Paris.

Né le 19 mars 1900 à Paris, Frédéric Joliot a fait ses études d'ingénieur à l'École de Physique et de Chimie industrielles de Paris. Dans cette école il a pu profiter de l'enseignement de Paul Langevin, sur les conseils duquel il est entré en 1924 au Laboratoire Curie comme préparateur privé de Madame Pierre Curie.

Dans les premières années de son activité scientifique, Frédéric Joliot s'intéressait à la confection de minces écrans métalliques dans le but d'étudier leur conductibilité électrique. Depuis son mariage en 1926 avec Irène Curie, F. Joliot a commencé à s'intéresser aux problèmes de radioactivité et en 1930 il a soutenu sa thèse de doctorat ès sciences sur l'étude électro-chimique des radioéléments.

Esprit clair et méthodique il avait le don d'imaginer rapidement des expériences simples qu'il exécutait avec grande ingéniosité et habileté.

C'est entre 1932–34 qu'ensemble avec Irène Curie il a publié une suite de travaux remarquables qui dépassaient le cadre de la radioactivité proprement dite. En irradiant des cibles de glucinium par les particules α et en étudiant les radiations très pénétrantes signalées par Bothe et Becker en 1930, I. Curie et F. Joliot ont observé un nouveau phénomène très surprenant : un écran de paraffine placé dans le trajet de la radiation pénétrante devenait lui-même le siège d'une émission de protons de grand parcours, qu'ils expliquaient comme un effet photoélectrique de photons d'environ 50 MeV. sur les protons. L'observation de la projection des protons était importante pour la découverte du neutron, signalé peu de temps après par J. Chadwick sur la base d'expériences plus détaillées sur d'autres noyaux légers projetés dans différents écrans par le glucinium irradié par les particules α. Frédéric et Irène Joliot-Curie ont pu montrer à la suite le neutron était plus lourd que le proton.

Presque simultanément avec ces travaux I. Curie et F. Joliot ont fait des travaux importants sur l'annihilation du positon dans la rencontre avec un négaton et sur l'effet inverse, la création d'une paire négaton-positon dans la rencontre d'un photon γ pénétrant avec un noyau atomique lourd.

La découverte la plus remarquable de Frédéric et Irène Joliot fut celle de la radioactivité artificielle, couronnée par le prix Nobel de chimie en 1935. En irradiant des métaux légers, comme par exemple l'aluminium, par les rayons α, les époux Joliot ont observé que l'émission simultanée de neutrons et de positons cessait pour les neutrons, mais continuait à se produire pour les positons quand on enlevait la source α. L'intensité de l'émission des positons décroissait avec le temps comme le ferait une source radioactive naturelle. E. Fermi et ses collaborateurs ont pu bientôt étendre la radioactivité artificielle aux éléments émetteurs de négatons en bombardant des noyaux légers ou moyens avec des neutrons lents.

F. Joliot a fait des contributions expérimentales élégantes à l'étude de la fission de l'urane après capture d'un neutron. Avec Halban et Kowarski il a annoncé que la fission de l'urane est accompagnée de l'émission d'environ trois neutrons, ce qui a laissé entrevoir la possibilité d'une réaction en chaîne et la libération massive de l'énergie nucléaire. En 1940, Frédéric Joliot fait venir en Angleterre son important stock d'eau lourde provenant de Norvège.

Joliot est élu membre de l'Académie des Sciences de Paris en 1943. Pendant plus d'un an il est directeur du Centre National de la Recherche Scientifique, et il est nommé Haut-Commissaire au Commissariat à l'Énergie Atomique en 1945, dont il doit abandonner la direction en 1950 pour des raisons politiques. En 1956 il succède à Irène Joliot-Curie comme professeur à la Sorbonne et il devient directeur du Laboratoire Curie et des Laboratoires de Physique Nucléaire nouvellement installés à Orsay, près de Paris.

Pendant l'occupation Frédéric Joliot a milité dans la résistance ; pendant plusieurs années il a été président du Conseil Mondial pour la Paix.

Frédéric Joliot avait des manières simples et il était d'un abord facile. Quoique très tourmenté intérieurement, il avait une nature gaie et il se liait facilement d'amitié. Un deuil cruel frappe sa fille Hélène Langevin son fils Pierre et ses proches.

S. Rosenblum

Sir Douglas Mawson, O.B.E., F.R.S.

When towards the end of 1907 Ernest Shackleton passed through Australia on his way to the Southern Continent, the Australian Government gave him £5,000 towards the expenses of his venture, and in return he undertook to take Australian scientists with him. In doing so, they unwittingly turned the Pole-seeking quest of a gentleman adventurer into an expedition of major scientific importance. This same gift was also responsible for the introduction to polar exploration of the man who was destined to inspire and lead the first major Antarctic expedition in which adventure was subordinated to scientific inquiry. When *Nimrod* left Lyttelton, Douglas Mawson was a geologist already mature in experience and a lecturer in the University of Adelaide. In the next fourteen months he was destined to accompany his mentor, Edgeworth David, to the summit of Mt. Erebus through autumn frost and blizzard and to the South Magnetic Pole deep within the Antarctic plateau and back to the coast, a journey which involved well over a thousand miles of man-hauling of the severest kind.

Scott would have welcomed him on his final venture, but Mawson had finished with pole-seeking and had other fish to fry. In 1911 he left Australia with a well-found party sufficiently strong to man two bases the common objective of which was the scientific exploration and annexation of as much of the Antarctic coast south of Australia as could be covered in two years. With him he had the first air sledge and the first wireless installation ever to be established in Antarctica. In March 1913, this station, in spite of gales averaging 50 miles an hour for month on month—for he had chosen as his main headquarters the stormiest region of the whole landmass, where katabatic gales sweep downwards to the coast throughout the year—transmitted direct to Australia that first dramatic message recording Mawson's return from an ordeal I believe no other

man I have known could have survived. After losing one companion and practically all the party's food down a crevasse and seeing a second companion die of starvation and over-exertion by his side, he cut his tent down to half a tent, his sledge down to half a sledge and trudged into his headquarters after three further weeks man-hauling alone on just enough food to keep body and soul together.

It is a measure of Mawson's courage and determination that his second enforced year's stay saw the carrying through of scientific work as fine in quality as that of the preceding year when all was going well. A stream of memoirs that kept the Australian Government Press busy off and on for forty years is one fitting tribute to an enterprise brilliantly planned and executed in the face of exceptional difficulties.

In the years following 1913 Mawson did outstanding work as field geologist and teacher; but Antarctic science remained a major interest throughout a long life that came to an end on October 15. He went to Antarctica again in 1929 and 1930, when he discovered MacRobertson Land, Queen Elizabeth Land and the Mackenzie Sea, using a seaplane to increase his range of action. Since the Second World War he has been a driving force behind the Australian Antarctic organization, A.N.A.R.E. When Prince Philip visited Australia in *Britannia* in 1956, it was Mawson who took the chair at the Antarctic symposium that was one important feature of the Melbourne programme, and the paper he delivered showed that his interest was as strong as ever and his intellect as keen. In courage, determination, singleness of purpose, breadth of scientific interest and quality of mind, he was Australian man at his best and he will be sorely missed. No one will regret his passing on more than the few surviving companions of his early adventurous days.

Raymond Priestley

Prof. F. A. Paneth, F.R.S.

Workers throughout the world in many branches of science have learned with deep regret of the death in Vienna on September 17 of Dr. Friedrich Adolph Paneth, a director in the Max-Planck-Institut für Chemie in Mainz and emeritus professor of chemistry in the University of Durham.

Paneth was born in 1887 in Vienna, where his father was lecturer in physiology in the University. After studying science at the University of Vienna, he moved to Munich and, later, to Glasgow, where he worked for a year in the laboratory of Frederick Soddy. In 1912 he was appointed assistant at the Vienna Radium Institute, and six years later to a chair at the Prague Institute of Technology; during the ensuing fifteen years he held similar posts in the Universities of Hamburg, Berlin and Königsberg. The events of 1933 in Germany caused him to leave that country and to seek refuge in London, where accommodation was found for him at the Imperial College of Science and Technology; the welcome he received there was later put on a more formal basis by his appointment to a readership in atomic chemistry. In 1939, Paneth was appointed to the chair of chemistry at Durham, from which he retired in 1953 on reaching the age-limit. Even then he was not content to give up active scientific work, but returned to Germany to take up the post at Mainz which he held until his death.

Paneth's early education had been broadly based—to the end of his life he retained a keen interest in the humanities—and he was never in danger of too narrow a specialization in his work. His first major contribution, dating from his time at the Vienna Radium Institute, was made when he and Hevesy laid the foundations of the modern use of radioactive isotopes as tracers. At that time, of course, only lead and bismuth among the common elements were available in a usable radioactive form; but Hevesy and Paneth not only demonstrated that such materials could be used to follow the details of chemical reactions, but also went on to investigate in some detail the behaviour of trace quantities of such substances in precipitation, adsorption, electrochemical and colloid experiments.

After leaving Vienna, Paneth continued with this fundamental radiochemical work, but he was also led, by one of those almost accidental steps which not infrequently precede big developments in science, to the experiments which conclusively demonstrated the transitory existence of the simple aliphatic free radicals—perhaps his most important contribution to pure chemistry. He had been using the extreme sensitivity of the radioactive indicator technique to demonstrate the existence of the hydrides of lead and bismuth, and went on, with Hofeditz, to examine the pyrolysis of tetramethyl lead carried, in a stream of hydrogen, rapidly through a heated quartz tube. They demonstrated, in a classic series of experiments, that the immediate products of the pyrolysis are metallic lead and free methyl radicals, and established a procedure that has since found wide use in studies of free radicals. During this period he was also refining the technique of measurement of the very small quantities of helium formed—as α-particles—in radioactive decay processes. This work was continued after Paneth's arrival in Britain, and increasingly applied to the problem of 'age determination', especially of meteoritic materials. He began also to turn his attention to some chemical aspects of meteorology and, in collaboration especially with E. Glueckauf, much careful work was done on the concentrations of the minor constituents of the atmosphere.

On account of the Second World War, Paneth achieved little in Durham until 1945, when he returned from Montreal, where he had spent two years with the joint British–Canadian Atomic Energy Laboratory to which he had been seconded. He was determined to set up in Durham a research laboratory devoted to radiochemical studies and, with characteristic indifference to the administrative difficulties of the immediate post-war period, he achieved his aim: the Londonderry Laboratory for Radiochemistry was formally opened in June 1947. Here the work on the rare gases, which was now Paneth's main interest, was pressed forward, with especially intensive work on the problem of the ages of meteorites. The atmospheric work was also continued, in collaboration with the U.S. Air Force, which carried out experimental rocket firings to obtain samples of air from very great heights for analysis.

Paneth was keenly interested in the history and philosophy of science (and, indeed, in philosophy in wider contexts) and was often consulted about the naming of newly discovered elements, and other questions of chemical nomenclature. As president (from 1949 until 1955) of the Joint Commission on Radioactivity of the International Council of Scientific Unions, he provided a useful link between the physical and chemical approaches to problems of standardization in radioactivity. In 1926 he had

been George Fisher Baker Lecturer at Cornell University, and his lectures formed the basis of his book, "Radioelements as Indicators"; with Hevesy he was the author also of "A Manual of Radioactivity", long regarded as a standard work on classical radioactivity. Paneth was elected to the Royal Society in 1947, and was honoured by many other learned societies, both in Britain and abroad.

It is clear that on his record as a scientist, Paneth is assured of a place in history, but something remains to be said of him as a person. He would not have counted himself a great experimentalist; rather his contribution was to create the conditions in which good work could be done—by selecting a happy team of collaborators, ensuring that they were not impeded by lack of equipment, and providing the necessary intellectual stimuli. He knew how to delegate responsibilities, and his colleagues knew that they could rely on his loyal support in anything they did on behalf of the Laboratory. Paneth was a natural linguist, and his command of English was extraordinarily good for one thrust into its use at so late a stage in his career. He was greatly in demand as a lecturer, and had a particular flair for exposition at the non-specialist level. These lectures were prepared with great care, and they were masterpieces of presentation, with just the correct blend of history, philosophy, wit, and hard scientific fact.

Paneth was a man of great personal charm—he can, for example, have had few peers in the matter of persuading museum curators to part with samples of meteorites—and he was blessed with a keen sense of humour. The numerous visitors to his Laboratory who enjoyed the hospitality provided at his home will long cherish memories of evenings of stimulating and amusing conversation. Their deepest sympathy will be extended to his widow, and to the son and daughter who survive him. G. R. MARTIN

NEWS and VIEWS

Nobel Prize for Chemistry: Dr. F. Sanger, F.R.S.

DR. FREDERICK SANGER, who has been awarded the Nobel Prize for Chemistry for 1958, is a member of the staff of the Medical Research Council, and has spent the whole of his research life in the Department of Biochemistry, University of Cambridge, the University of which he was an undergraduate. The award has been made for his researches on the structure of the protein hormone insulin, the elucidation of which he completed in 1955, at the age of thirty-seven, after ten years of intensive research. The methods which he developed for this purpose are a model of effectiveness. When he began his investigations on insulin, Dr. Sanger first devised the use of dinitrofluorobenzene for the identification and estimation of the free amino-groups of proteins or peptides, and this method has since been widely adopted. By 1949 Sanger had shown that oxidation of insulin with performic acid, to break disulphite bonds, led to two separate fractions. Partial hydrolysis of the two separated portions with acid, and later with enzymes, yielded a series of peptides which he isolated by chromatography. The application of the dinitrofluorobenzene method to the peptides enabled Sanger and his colleagues to determine the sequence of amino-acids in the peptides, and so to deduce the sequences in the two large portions which had been formed by the oxidative fission of the insulin molecule. The results were such that a unique sequence of amino-acids could be ascribed to each of the two portions of the molecule. The determination of the position of the disulphide linkages involved the subjection of insulin to partial hydrolysis by enzymes under conditions in which the disulphide bonds remained stable. The cystine-containing peptides in the hydrolysate were separated and their structures determined by the methods he had previously developed. The structures of the cystine peptides which thus were elucidated showed that only one solution was possible to the problem of the distribution of the sulphide bonds in insulin. Two of these formed junctions between the two main peptide chains of the molecule, while a third disulphide link spanned four amino-acid residues in a manner similar to that previously deduced by du Vigneaud and his colleagues for the hormones oxytocin and vasopressin. Afterwards, Sanger and his colleagues showed that certain of the amino-acids within this intra-chain disulphide link differ in insulins from different species. Dr. Sanger's methods and example have stimulated much research in the investigation of protein structure, the limits of which have yet to be visualized, and they make clear the possibility that insulin may be completely synthesized in the laboratory, although this is unlikely to occur for some time to come.

Nobel Prize for Physics: Dr. P. A. Čerenkov, Dr. I. M. Frank and Dr. I. Tamm

THE award of the Nobel Prize for Physics for 1958 to the Russian physicists, P. A. Čerenkov, I. M. Frank and I. Tamm, for their work in the discovery and interpretation of the nature of Čerenkov radiation, is a fitting recognition of a scientific advance which has acquired great importance for experimental high-energy nuclear physics and cosmic rays. Čerenkov's contribution was to make, in 1934, a detailed study of the light emitted by liquids when they were exposed to radiations from radioactive substances. That certain substances were fluorescent under the influence of such radiations had been known since the days of Becquerel, but whereas fluorescent light depended markedly on the chemical nature of the substance, a weak residual light was found to be emitted even when all traces of fluorescent substances had been removed. This light was named the Čerenkov light; it was given a theoretical interpretation by Frank and Tamm in 1937. Frank and Tamm showed, on the basis of classical electromagnetic theory, that a charged particle travelling through a medium with a velocity greater than the velocity of light in that medium gives rise to an electromagnetic shock wave. This shock wave, which is analogous to the bow wave produced in water by a fast-moving ship, constitutes the Čerenkov radiation. Čerenkov light can only be observed in a medium which has a sufficiently high refractive index to bring the velocity of light in the medium below that of the charged particle; and it is emitted (like a bow-wave on water) at a definite angle to the direction of motion of the charged particle, the angle

being a function of particle velocity. Modern Čerenkov counters make use of these properties to distinguish between particles of different velocities which emerge from the targets of the giant particle-accelerating machines.

Atomic Energy Patents: Mr. J. A. Gay

Mr. J. A. Gay has been appointed patents exploitation officer to the United Kingdom Atomic Energy Authority in succession to Mr. T. Benson Gyles. Mr. Gay, who is thirty-six and graduated at University College, London, was formerly in the Commercial Department of the Authority's Industrial Group. In 1949 he was appointed development engineer to Standard Telephones and Cables, and in 1951 joined Messrs. O. W. Roskill, industrial consultants, as senior engineer. During 1953–56 he was with Isotope Developments, Ltd., and in 1956 joined the Authority's staff at Risley. Inventions developed in the course of atomic energy work and which are available for commercial exploitation continue to be filed at the rate of about eight a month. Many of them may be applied in a wide variety of industries, both inside and outside the atomic energy field, and the total number of inventions available for use by firms is now more than 400.

U.S. International Co-operation Administration: Visit to Africa

The U.S. International Co-operation Administration is the organization through which the U.S. Government channels its funds for aid, of all kinds, to the different countries of the world. The Administration is the successor to the various agencies which have fulfilled this role since the days of the Marshall Plan and is closely associated with the U.S. State Department. For some months, the Administration has been exploring the possibilities of greater utilization of the scientific resources of the United States, and other countries, in attacking the problems of under-developed countries and territories, particularly in tropical Africa. The director of the Administration, Mr. James H. Smith, has started this week on a tour throughout tropical Africa, to examine on the ground the scientific work which is in progress. He is accompanied by Mr. Joseph C. Satterthwaite, recently appointed Assistant Secretary of State for African Affairs in the State Department, Dr. J. G. Harrar of the Rockefeller Foundation, Dr. Richard Bradfield, agronomist of Cornell University, and Dr. John M. Weir, who is working on tropical medicine for the Rockefeller Foundation. The Administration recently informed the Lord President's Office that Mr. Smith hoped to include two scientists from the United Kingdom in the party. In response to this invitation, arrangements have been made for Prof. G. B. Maegraith, professor of tropical medicine, University of Liverpool, and Mr. Dunstan Skilbeck, principal of Wye Agricultural College, to fly out this week to Africa and join Mr. Smith's party. The itinerary starts in Liberia and proceeds through Ghana, Nigeria, Kenya, Ethiopia, Sudan and Tunis.

Commonwealth Fellowships

The new scheme for Commonwealth Fellowships, announced at the Montreal Conference in September, was warmly welcomed in both Houses of Parliament in the debate on the Queen's Speech on October 28 and 30. The scheme provides for 1,000 scholarships a year and Great Britain has announced her willingness to take half, while at the same meeting Australia announced that she was increasing her scholarships under the Colombo Plan by 150. There are now 38,000 Commonwealth and overseas students in Great Britain compared with 10,000 in 1951, and 10–12 per cent of all places in British technical colleges are occupied by overseas students, two-thirds of whom come from the Commonwealth: at the Imperial College of Science and Technology the percentage of overseas students is 38 and at the British Postgraduate Medical Centre, 60. Earl Jellicoe, in welcoming the scheme, referred to the crucial importance attached to education by all Commonwealth countries at Montreal and to the need for Britain to remain a great reservoir of humane wisdom and technical knowledge on which the Commonwealth and the free world could draw. Mr. P. Maitland particularly welcomed the assurance that these 1,000 scholarships for the interchange of Commonwealth advanced students would cover the humanities as well as science and technology; and Mr. J. Dugdale referred to the asset which such scholarships represented in Commonwealth relations and also to the value of an inter-Commonwealth service of technical experts.

National Science Foundation: Research for Teachers and Travelling Lectures

The U.S. National Science Foundation has invited universities, colleges, and other non-profit institutions with appropriate research facilities to submit proposals for support of Research Participation Programmes for Teacher Training. It is planned to support a limited number of experimental programmes which will provide research experience during the summer months for teachers of science and mathematics in high schools and small colleges, under the guidance of experienced scientific investigators. Courses combining laboratory experience with seminars on scientific subjects and research techniques will be provided with the objective of improving science teaching. Support will be provided by the Foundation for stipends and travel for approximately 700 teachers and for expendable supplies, secretarial and administrative expenses, and other institutional costs directly attributable to the teacher training aspects of the programmes.

The National Science Foundation is also to expand its programme of travelling science demonstration lectures, previously administered solely by the Oak Ridge Institute of Nuclear Studies, Tennessee, to include a few regional centres throughout the United States. Individuals will be selected by the regional centres to receive three summer months of intensive training designed to prepare teachers to give lecture-demonstrations in physics, chemistry, biology or mathematics in a number of high schools during the school year 1959–60. Emphasis is on fundamental scientific principles which can be demonstrated by simple equipment which teachers can construct. Each travelling lecturer will spend three to five days at 30–40 representative secondary schools throughout the area served by the regional centre, giving demonstrations using the special equipment which they carry with them, and assisting local science teachers.

Unesco Research Ship

A proposal that Unesco should sponsor an international research ship was strongly supported by a group of international marine scientists who have

just concluded a series of meetings in Paris. The meeting was called to discuss Unesco's role in promoting international co-operation for oceanic exploration and was attended by consultants from scientific organizations in Australia, Denmark, Finland, France, the German Federal Republic, Italy, the Netherlands, Norway, Poland, Sweden, the United Kingdom, the United States and the U.S.S.R. The ship, it was pointed out, would supplement research already being carried out on a national basis by some of the larger countries and could also tackle oceanographic problems that cannot be undertaken by the existing ships. To meet this task, it was suggested that the ship should be of about 1,200–1,300 tons and some 220 ft. long. Laboratory space would be provided for six permanent scientists and additional accommodation for fifteen visiting experts and students in training. A supplementary proposal recommended that Unesco should operate a number of chartered research ships on an international basis. Emphasizing the importance of increasing the food resources of the world by development of the oceans' potentialities, the consultants also urged that Unesco and the United Nations Food and Agriculture Organization should direct the attention of all governments to the importance of marine research. Further specific aid was requested from Unesco in the form of research contracts for individual workers and laboratories, fellowships for training purposes, travel allowances for scientists participating in international co-operative projects, the assignment of experts to countries requiring technical assistance in this field and the provision of equipment and facilities for co-operative projects between countries. These proposals are being submitted to the Director-General of Unesco for further examination.

McGill University, Faculty of Engineering

THE Faculty of Engineering of McGill University, in common with those of all other Canadian universities, is expecting a continuing growth in the number of applicants over the next decade, and is also anxious to encourage postgraduate studies to a greater extent than hitherto. The present buildings have been basically unchanged for some fifty years, although during that time, and particularly since 1945, relatively small additions have been made to accommodate the increased number of students admitted. In the session 1957–58 there was a total of some 1,800 undergraduate students in the Faculty, which represented the absolute maximum that the present buildings could take. In May 1958 ground was broken for a new engineering building to supplement the present facilities. This building, with an area of some 140,000 sq. ft., has been designed to provide lecture rooms and drafting rooms, particularly for the students in the earlier non-specialized years of the course; to give, for the first time, proper quarters to the School of Architecture, and to provide completely new quarters for the Department of Electrical Engineering which was formerly housed in the old building. The release of this space from the old building will permit expansion of the Departments of Mechanical and Civil Engineering, where heavy installed equipment made it preferable to expand *in situ* rather than move into completely new quarters.

Mr. J. W. McConnell, the senior governor of the University, has made a magnificent gift which will cover the complete cost of this new building, which is expected to be opened in October 1959. The extra space then made available will make it possible for the faculty to embark upon a programme aimed primarily at the development of honours and graduate students in engineering, as well as permitting improvement in the quality of, and a small increase in the numbers admitted to, the ordinary engineering courses. The programme leading to the development of graduate work is already under way, and it is hoped soon to make appointments to three new chairs which have been created in control engineering, mining engineering and applied mechanics, and propulsion. It is also hoped that in the next few years a number of additional chairs will be created so that full use can be made of the new facilities.

Higher Education in the United Kingdom

THE revised edition of the handbook for students from overseas issued by the British Council and the Association of Universities of the British Commonwealth under the title "Higher Education in the United Kingdom" (pp. 208. London: Longmans, Green and Co., Ltd., 1958. 5*s*.) contains much useful information. Thus it includes, besides a dictionary of subjects and facilities for study and the lists of addresses of universities, technical colleges and other institutions, which occupy the greater part of the handbook, tables of fees and notes on the cost of study and residence, and on life in a British university or technical college. There is a foreword by Dr. R. S. Aitken, and a short article on universities in the United Kingdom by Sir James Mountford and another on technical education by Dr. P. F. R. Venables. The handbook brings together much information of great value not merely to overseas readers but also to those in Britain who are concerned with advising and placing students.

British Commonwealth Collections of Micro-organisms

THE United Kingdom National Committee of the British Commonwealth Collections of Micro-organisms is about to prepare a new edition of the "Directory of Collections and List of Species maintained in the United Kingdom and Crown Colonies". Directors of laboratories whose names appear in the 1951 edition will be asked to revise the information given in that directory, and to supply lists of micro-organisms now available for distribution. Other laboratories may have established general or specialized culture collections since the 1951 Directory was prepared, and if they are willing to make their cultures available to other interested workers they are asked to send lists before December 31 to Dr. S. T. Cowan, Secretary of the U.K. National Committee, at the National Collection of Type Cultures, Central Public Health Laboratory, Colindale Avenue, London, N.W.9.

Library Classification

A scholarly address, "Library Classification and the Field of Knowledge", delivered by Mr. D. J. Foskett at the annual general meeting of the North Western Group of the Reference and Special Libraries Section by the Library Association in Manchester, on February 26, has been issued by the Association as Occasional Paper No. 1 (pp. 15. London: Library Association, 1958. 2*s*. 6*d*.). Systems of classification, Mr. Foskett shows, arise not empirically merely as a practical convenience but as reflexions of the state of scientific and philosophical thought in any age,

bringing together these parts of the field of knowledge that are seen to be clearly related. One must always be prepared to amend or overthrow existing systems which fall short of the requirements. Such discord as exists between the general classification systems and the requirements of modern research should not be allowed to continue.

Siemens Edison Swan Journal

The format of the first number of the *Siemens Edison Swan Journal* (1, Summer 1958. Pp. 1–64. London: Siemens Edison Swan, Ltd., 1958) is remarkably good, as also the standard of the six articles which make up the contents. Tear-off abstracts in English, French and German complete with universal decimal classification numbers are provided. The *Journal* has been launched, the managing director, Dr. J. L. Aldington, says in his foreword, in order to provide additional opportunities for the staff to announce their achievements, and in one sense will supplement the technical press and journals of the learned societies, which from time to time include original contributions from the Company's staff, and in another sense will replace the old *Siemens Engineering Bulletin* by a more permanent and comprehensive record of the Company's contribution to electrical technology. The articles include a description of the "Centenary Neophone", a completely new telephone handset which the Company has recently produced, the main features of which are printed wiring, improved performance at lower cost, and reduction in size and weight; a review of recent applications in the light electrical engineering and cable industry; a brief discussion of some photoconductivity effects in grown crystals, particularly cadmium sulphide; and a survey of the manufacture of grids for radio valves.

Biochemical Pharmacology

The first number has recently been published of a new international journal, *Biochemical Pharmacology* (1, No. 1; July 1958. Pp. 104. Subscription, including postage: (*A*) £6 (U.S.A. 17 dollars); (*B*) for subscribers certifying that the journal is for their own personal use, £5 5*s*. (15 dollars per annum). Four issues per volume. London: Pergamon Press, 1958). The journal will be devoted to "research into the development of biologically active substances and their mode of action at the biochemical and sub-cellular level". It will be under the guidance of an editorial advisory board containing many distinguished names from Europe and America. Papers will be in English, French or German. Short communications for quick publication will be accepted as well as full-length papers. It is intended to give emphasis to cancer chemotherapy and related studies, and this policy is reflected in the series of papers published in the first issue.

The Lichenologist

A new society, the British Lichen Society, founded early in 1958 to encourage the study and conservation of lichens, and conscious of the need to make up for past neglect of this interesting group of plants on the part of contemporary botanists, has now issued the first number of its journal, *The Lichenologist* (*Curator*, Dr. T. D. V. Swinscow, Everley, London Road, Knebworth, Herts.; *Hon. Secretary*, A. E. Wade, National Museum of Wales, Cardiff. Annual subscription and journal, 20*s*.). The major aims of the journal are to instruct and to communicate new information on taxonomic, distributional and ecological aspects. The first issue contains useful articles on the British species of *Cladonia* and *Collema*, notes on arctic–alpine and other lichens new to England, procedures for collecting and preserving lichens, and so on. This effort deserves the support of all who are interested in this group.

Foxboro-Yoxall's Training School

The training school started in 1951 by Foxboro-Yoxall Ltd. at Wandsworth has now been moved to Redhill, Surrey. These premises have a greatly increased capacity, but in order to maintain an individual approach, courses are at present limited to nine students. The courses are of three weeks duration and comprise a maintenance course (*A*), designed to give instrument mechanics with limited experience in industrial instrumentation, practical training in the use and maintenance of Foxboro equipment; an advanced instrument course (*B*), designed for technical instrument engineers and covering the theory of control instrumentation and its application to industrial processes. Special courses related to particular user industries are also given from time to time. These have recently included one on instrumentation in the paper industry and another on instrumentation for coal-washing plants.

Leprosy Research Fund

The Leprosy Research Fund was established in 1953, when Dr. R. G. Cochrane (of the Leprosy Research Unit, 11*a* Weymouth Street, London, W.1) was appointed technical adviser to the American Leprosy Missions, which had given financial aid to his researches on the histopathology of leprosy. The aim of the Fund is not to finance large research schemes, but to stimulate pilot research projects and inquiries. The Fund does not in any way compete with other organizations. It seeks, in fact, to help other organizations by indicating, through its pilot researches, problems that are sufficiently important to merit further consideration. The Fund also undertakes preliminary clinical trials of new drugs likely to be useful for the treatment of leprosy. For investigations of this kind only advanced lepromatous cases are taken, and the Fund is in touch with institutions all over the world. The Fund has studied the histopathology of leprosy for several years and has been able to supply workers with typical histological pictures of the various types and groups of leprosy. The Fund proposes to establish a unit containing a registry of clinical, photographic and histological records of the various types and groups of the disease, together with sets of slides, so that a world picture of the disease may be obtained for reference. It is estimated that the cost of such a unit will be about £2,300 a year.

National Museum of Wales

The National Museum of Wales has recently issued a new edition of its "Illustrated Guide" (pp. 39+ 2 plates. Cardiff: National Museum of Wales, 1958. 1*s*. 6*d*.). It is, indeed, more than a new edition, for the subject-matter has been entirely re-cast and new illustrations have been included. The format is interesting and attractive and the typography clear and easy to read. Following a few notes on the building, well illustrated by clear plans, each depart-

ment is dealt with in rotation but on a common plan. The purpose and policy of each is stated and brief allusion is then made to the chief exhibits. The "Illustrated Guide" is completed by an impressive list of publications and the whole is a model of what museum guides should endeavour to be.

Gibberellic Acid-like Substances in Higher Plants

As earlier studies have shown, gibberellic acid has notable growth-promoting effects when applied to dwarf varieties of *Pisum*, *Phaseolus* and maize, whereas tall varieties may be little affected. In an investigation of the distribution of substances similar to gibberellic acid in higher plants, M. Radley has demonstrated the presence of such substances in extracts made from seeds and from all parts of seedlings of tall and dwarf peas and from mature seeds of wheat and french beans (*Annals of Botany*, N.S., 22, 297; 1958). These substances were present in amounts equivalent to 0·1–0·3 μgm. gibberellic acid in 100 plants. It is stated that larger quantities were obtained from immature runner bean seeds, the substance being distributed between testas, cotyledons and embryos. A new biological test for gibberellic acid-like materials is described.

University News : Leeds

THE following gifts have been received among others by the University of Leeds: £1,500 to the Department of Inorganic and Structural Chemistry from the Royal Society for scientific investigations on high-resolution nuclear magnetic resonance spectroscopy; £700 to the Department of Botany from the Royal Society to purchase special equipment; £1,000 to the Department of Civil Engineering from the Cement and Concrete Association towards the postgraduate course in concrete technology; £2,715 to the Houldsworth School of Applied Science over three years from the Department of Scientific and Industrial Research for research on the brittle fracture of metals; and £500 from the Shell Group of Oil Companies for postgraduate research in chemical engineering; £700 a year for three years to the Department of Biochemistry from the Wellcome Trust for the salary and expenses of a research assistant.

The following have been appointed lecturers: Dr. P. B. Ayscough in the Department of Physical Chemistry; Dr. R. G. Burwell in anatomy; Dr. A. J. Kenny in biochemistry. The title of reader in textile physics be conferred upon Mr. H. J. Woods, senior lecturer in textile physics.

London

MR. F. H. LUDLAM, lecturer in the Department of Meteorology at Imperial College of Science and Technology, has been appointed to the readership in meteorology at the same College. The title of reader in aerodynamics in the University of London has been conferred on Mr. L. E. Fraenkel in respect of his post at the Imperial College of Science and Technology. The title of reader in biology in the University of London has been conferred on Dr. H. Kalmus in respect of his post at University College.

Sheffield

THE title of emeritus professor of zoology has been conferred on Prof. L. E. S. Eastham, who retired recently (see *Nature*, 181, 1307; 1958). The following appointments have also been made: Mr. P. R. Becker, to be lecturer in the Electronic Computation Laboratory; Dr. P. E. Brown, to be lecturer in geology.

Announcements

MR. J. TANKARD (British Rayon Research Association, Wythenshawe, Manchester) and Dr. F. O. Howitt (Wool Industries Research Association, Leeds) have been awarded Service Medals of the Textile Institute. The Service Medal was first awarded in 1940 and is given for valuable services rendered to the Textile Institute.

STARTING with the January 1959 issue, Consultants Bureau, Inc., is undertaking the translation of all non-English articles appearing in each issue of the *Czechoslovak Journal of Physics* (annual subscription: 6 issues, 50.00 dollars). Further information can be obtained from Consultants Bureau, Inc., 227 West 17th Street, New York 11.

A SYMPOSIUM on "The Chemistry of Co-ordination Compounds", organized by the National Academy of Sciences, India, will be held in Allahabad on February 7 and 8. Further information can be obtained from Dr. Arun K. Dey, Department of Chemistry, University of Allahabad, India.

IT is proposed to hold a symposium on "Cultural and Metabolic Aspects of Moulds", organized jointly by the Society for Applied Bacteriology and the Istituto di Sanita in Rome in the spring of 1960. The symposium will be open to *bona fide* workers in this field whether they are members of the Society or not. Those interested should write to Mr. G. Sykes, Boots Pure Drug Co., Ltd., Microbiology Division, Standard Department, West Bridgford, Nottingham, as soon as possible.

AN international symposium on antibiotics will be held in Prague during May 17–23. The proceedings will be divided into three sections, dealing with problems of the biosynthesis of antibiotics; the scientific pathophysiological basis of antibiotic therapy; and the problems of fermentation technology and non-medical use of antibiotics. Further information can be obtained from the secretary of the symposium, Dr. M. Heřmanský, Antibiotics Research Institute, Roztoky, near Prague, Czechoslovakia.

A JOINT endocrine meeting will be held at the Royal Society of Medicine on April 24 and 25, 1959. It will be sponsored by the Section of Endocrinology of the Royal Society of Medicine and the Society for Endocrinology with the participation of the Society for the Study of Fertility, the Medical Section of the British Diabetic Association, the London Thyroid Club and the Endocrine Club, Glasgow. Short papers will be read and a dinner will be held on April 24. Further details can be obtained from the Honorary Secretary, Section of Endocrinology, Royal Society of Medicine, 1 Wimpole Street, London, W.1.

ERRATUM. In the communication entitled " 'Solubilization' of a Cytochrome *b* Component from *Micrococcus lysodeikticus*", by F. L. Jackson and Valerie D. Lawton in *Nature*, 182, 799 (1958), para. 3, line 7, for "529–530 mμ" read "429–430 mμ". This was overlooked in proof by the authors.

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE

THE formal opening of the new University Chemical Laboratory in Cambridge by Princess Margaret on November 6 marks a deeply significant change in the topographic distribution of the University science laboratories. Hitherto, these had been compactly—in fact, all too compactly—built on each side of the Pembroke Street – Downing Street axis, physics, chemistry and zoology being on the north side of this axis, and geology, mineralogy and the other biological sciences on the south side of Downing Street. The Chemical Laboratory was originally built in 1887 at the corner of Pembroke Street and Free School Lane, but required several additions as the numbers of students increased: the two major additions occurred in the early 1920's, when the new organic wing was built with a considerable grant from the British oil companies, and when physical chemistry occupied the building in Free School Lane vacated by the Engineering Department. At the end of the Second World War, the Chemical Laboratory, by virtue of this piecemeal and improvised growth, had lost its original design and had become both inconvenient and uneconomic (in man-power and material) to run, was congested with students, and lacked space to house the modern equipment which it so badly required. The decision to migrate from the traditional science centre to the new site in Lensfield Road was based primarily on the virtual impossibility of rebuilding adequately on the old site, and also on the value of this site for the subsequent expansion of its cramped neighbours: the means for this migration were provided by a sympathetic Government Grants Committee, supported on the personal side very largely by the vigorous and steadfast appreciation of the position by Sir Alexander Todd.

The new laboratories consist essentially of two long rectangular blocks running parallel to Lensfield Road in an east–west direction, the block nearer to Lensfield Road accommodating the Department of Physical Chemistry and the other more distant and higher block accommodating the Department of Organic and Inorganic Chemistry. The two blocks are joined at the western end by a narrower block, which houses an additional part of physical chemistry, and also theoretical chemistry, spectroscopy, the library, administrative offices and canteens.

Between the two main blocks, on the ground floor, are two lecture-rooms each holding about 200 students, and a third lecture-room, to hold 450 people, is being added for both departmental and general University purposes.

At the east end of the organic–inorganic block an L-shaped extension is being constructed to provide extra research facilities and to accommodate the first- and second-year students in these branches of chemistry. When this extension becomes available, the migration of all chemical teaching and research from Pembroke Street to Lensfield Road will be complete, and the University of Cambridge will possess one of the most commodious and best-equipped laboratories for chemical teaching and research in the United Kingdom.

The main organic–inorganic block was constructed first and has now been in occupation for some time. The central portion consists of a basement which houses the store-room, workshops and (at the east end) the central heating station; the ground floor is devoted to third-year organic teaching, the first and second floors to organic research, the third floor to inorganic and radiochemical research, and the fourth floor contains the plant room for the mechanical services, particularly those for the ventilation of the building and for the fans.

The central portion of the main physical chemistry block has a basement which contains the store-room, workshop and research accommodation, two floors devoted to teaching, a third floor to research, and a fourth floor which also houses a plant room.

The gross floor area of the complete building will be approximately 238,000 sq. ft.

The construction of the two major blocks embodies a number of novel features. In particular, the steel frame is built up of horizontal lattice girders, each about 45 ft. long × 3 ft. deep, welded together side by side to form a continuous frame on which each floor is constructed from pre-cast concrete slabs and a 3-in. concrete screed. These girders span the entire width of the blocks without internal columns, and thus allow the large teaching laboratories on the lower floors to be completely unobstructed, while on the research floors above considerable flexibility for subdivision is possible. The wall piers are of composite steel and concrete construction, the external walling being otherwise of 13½-in. solid brickwork faced with brown Buckinghamshire bricks.

The space within the lattice frame of each floor contains the horizontal runs of electrical and mechanical services. Hot-water heating pipes, which are attached to the underside of the frames, form, with removable aluminium panels, the heated Frenger ceilings.

The research floors have a central corridor, 6 ft. 9 in. wide, with rooms and laboratories on each side assembled on a modular basis, each module being fully serviced; these research laboratories are separated by fireproof reinforced plaster panel partitions, which being non-structural are removable, so that the number of moduli forming any laboratory can be changed without undue trouble.

All laboratories are supplied with cold water at high and low pressure, with hot water (maximum temperature, 65° C.), distilled water, gas and compressed air (15 lb./sq. in.); certain laboratories are also provided with high-pressure air (100 lb./sq. in.), steam, reduced pressure (10 mm. mercury), and with oxygen. A water-softening unit, of capacity 400 gallons per hour, in the boiler house provides the water required for the steam generator, and for the automatic still which delivers distilled water into two 500-gallon polyethylene-lined storage tanks, whence it is fed through polyethylene pipes to all the individual laboratories. Polyethylene piping is also used to convey all cold effluent from the laboratory sinks, drip wastes, fume cupboards, etc., to the horizontal 4-in. bore cast-iron pipes which run through the

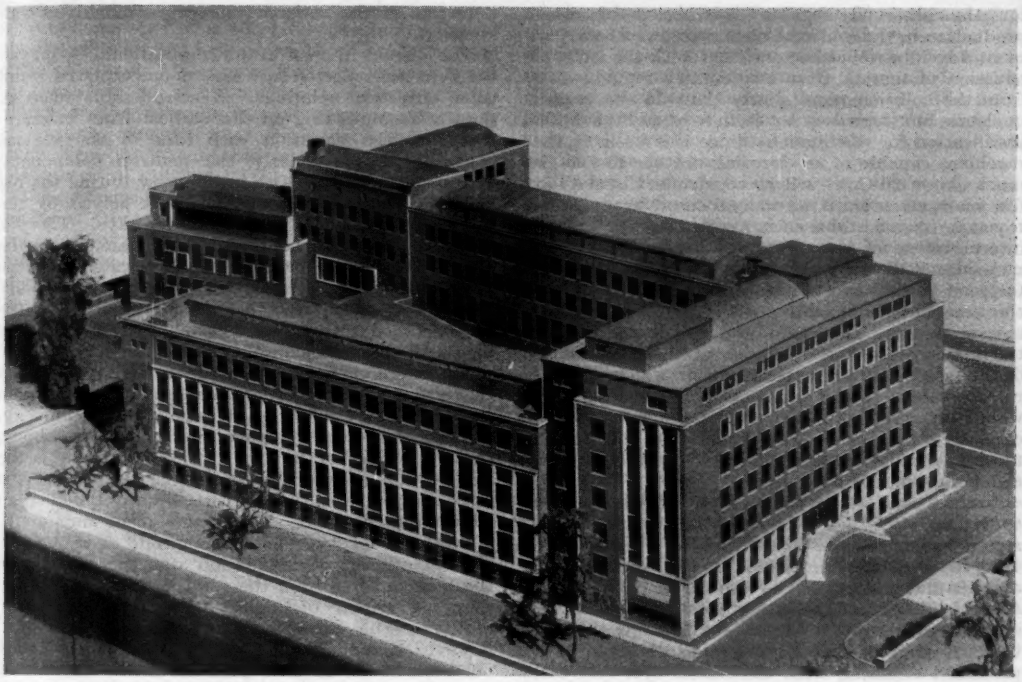


Fig. 1. University Chemical Laboratory, Cambridge. Photograph of the complete model of the Laboratory, viewed from the north-west. The main entrance is shown on the right. The long block in the foreground is occupied by the Department of Physical Chemistry, and that in the background by the Department of Organic and Inorganic Chemistry: the lecture rooms lie between these blocks. The two smaller blocks at the far left-hand corner are still under construction

lattice girders, and which are coated internally with acid-resisting plastic paint. Hot effluent from steam outlets is, however, carried through intermediate lead or stoneware piping.

To allow the desired flexibility in the size of the research laboratories, the teak bench tops are supported on cantilever brackets which fit into service racks designed to carry the tops at sitting or standing height, or to enable them to be completely removed. Independent cupboards of standard size but of various internal designs fit snugly beneath the bench tops: a research worker can thus choose a selection of cupboards suitable for his own work.

The design and construction of this Laboratory have presented many difficult and often novel problems. The University is particularly indebted to Mr. J. Murray Easton and Mr. S. E. T. Cusdin, of Messrs. Easton and Robertson, the architects, and to Mr. A. R. Gilson, the former superintendent of the Laboratory, who has closely and very effectively co-operated with them for the success of this project, which, in the hands of the contractors, Messrs. Kerridge and Co. (Cambridge), Ltd., and Messrs. Rattee and Kett, Ltd., has provided a chemical laboratory in which the University may well take great pride.

F. G. MANN

COSMIC RAYS

CONFERENCE AT DURHAM

A PHYSICAL Society Conference on "Cosmic Rays" was held in the Durham Colleges in the University of Durham on September 24 and 25. About one hundred delegates from most of the European centres of cosmic ray research gathered to discuss topics ranging from the cosmological significance of large extensive air showers to recent measurements of the cosmic ray intensity in deep Canadian mines.

The theme of the Conference was two-fold: the cosmic and geophysical significance of cosmic ray measurements, and the nuclear physics of single-particle interactions. The Conference was divided into short sessions in which an invited review paper of 45 min. was followed by a number of 10-min. papers.

The first session was devoted to a discussion of interactions in the energy-range 1–100 GeV. Recent results with machines were considered at the lower end of the energy region and the results of cosmic ray proton experiments for the remainder. Experimentally, several features appear to be clear: the inelasticity of proton interactions with light elements does not vary greatly with proton energy; the value is about 60 per cent, and the rate of production of heavy mesons increases slowly with increasing energy. Also clear is the inadequacy of the various theories of meson production—Fermi, Landau, etc.—to account

for the observed angular distribution of meson production in the centre of mass system. The experimental results would be consistent with the isotropic emission of mesons from two centres moving away from the collision more slowly than do the original nucleons, but there does not seem to be any theoretical justification for this model. Since it is unlikely that machines capable of accelerating protons to energies much above 20 GeV. will be constructed in the next few years, attention is naturally focused on the cosmic ray experiments in this energy region. At present the interpretation of the experiments is difficult: the momenta of the primary protons are not measured, in fact, often the directions are not determined, and the secondary momenta are too high for accurate measurements. This point was well brought out in the first contribution, which described the results of a design study for an experiment in which accurate measurements of the parameters of the interaction would be possible. Such an experiment would be expensive by cosmic ray standards but not by machine standards; it is perhaps within the scope of a collaborate university venture.

In the second session the energy-range was extended to 100,000 GeV. Most of the information in this region has come from studies of the so-called 'jets' observed in nuclear emulsions exposed in high-flying aircraft and balloons. The number of particles produced in the cascade resulting from some of the very energetic nuclear encounters (above a few thousand GeV.) is so great that the events can be seen in the processed emulsion with the naked eye. At these high energies there is quite copious production of particles heavier than the pion, for example, the ratio of the charged heavy particles to all charged particles is 18 ± 5 per cent. Another important result is that the interaction length of the secondaries of mean energy around 200 GeV. is very close to that found for pions and protons in the region of a few GeV. This result has important implications in the study of the development of the various components of the cosmic radiation through the atmosphere. Thus, for example, the pion flux is subject to the competing mechanisms of decay and interaction and is consequently sensitive to the value of the interaction length.

The energy-range under review was extended still further in the next session when various aspects of extensive air showers were discussed. The cosmological aspect is of supreme interest, bearing as it does on the origin of the cosmic radiation. The situation here has not changed over the past few years: the search for anisotropies in the primary cosmic radiation at energies up to 10^{18} eV. or so has still failed to produce statistically significant results. The need at present is for an order of magnitude increase in the size of the detecting arrays for extensive shower studies, and at least two such projects are afoot at the present time. Even with improved experimentation, however, the interpretation of the sea-level shower data is not straightforward. The electron component, which is traditionally measured, is subject to considerable fluctuations, arising in the main from the fluctuation in the height of the first primary proton interaction. For this reason attention is now being turned to the muon component for which the fluctuations are smaller, although difficulty is encountered due to the particle densities being considerably lower, at least for distances less than a few hundred metres from the shower core. The session finished with the description of a number of new techniques by which detectors of the necessary large area could be constructed.

The current interest in the International Geophysical Year was reflected by a session on cosmic rays and solar–terrestrial relations. A considerable mass of data is accumulating on this subject from measurements or the variation with time of the various components, particularly the neutron component. The spectacular increases in intensity during the big solar flares has emphasized the part played by the Sun in producing low-energy cosmic rays. There is as yet no completely satisfactory explanation of the way in which these particles are accelerated or of the modulation of the primary cosmic rays by the Sun's magnetic field, but the result of the analysis of the very detailed International Geophysical Year results may lead to a considerable advance.

The interaction of the primary cosmic rays with the Earth's magnetic field was discussed by speakers from the Imperial College of Science and Technology. Experiments over the past few years have shown that the position of the cosmic ray equator, that is, the locus of the minimum of the cosmic ray intensity, is not consistent with the magnetic equator based on an eccentric dipole field. The disagreement amounts to a westward displacement in longitude of about 45°, and an attractive explanation was the bending of the lines of force from the rotating Earth by a surrounding region of highly ionized interplanetary matter. The Imperial College group has shown, however, that the dipole approximation is not a good one even at the distance from the Earth where most of the magnetic deflexion of the primary cosmic ray takes place. A more accurate treatment of the effect of the Earth's field taking into account the various magnetic anomalies removes the discrepancy between the respective equators.

The development of the muon component through the atmosphere and below ground occupied the next session. It was demonstrated that measurements on the sea-level muon flux give information on the multiplicity and mass spectrum of the products of primary interactions. Comparison with the underground depth–intensity relation gives information on the energy losses of muons of energy up to 1,000 GeV.—information that is not available from other measurements.

With the introduction of new techniques of measurement, in particular the neon flash-tube of Conversi, and the consequent ease of measurement of high particle momenta, there has been something of a revival of muon spectrum measurements. Large magnetic spectrographs have been completed recently at sea-level at Cornell and Durham, and a number of smaller instruments are under construction for measurements of muon spectra in inclined directions and at various depths underground. The next few years should see significant advances in this subject.

The interactions of individual fast muons with nuclei were also discussed in this session. This interaction is via the flux of virtual photons accompanying the muon, and recent advances have been made both in the theoretical study and the experimental determination of cross-sections and other parameters of the interactions. Although there is still some slight doubt as to the way in which the original Williams–Weizsäcker treatment of the virtual photon flux is to be modified for ultra high-energy muons, the main features, such as the angular deflexions of the interacting muons and the multiplicity of the pion secondaries, are understood. The impor-

tance of these measurements lies in the fact that what is being studied is effectively the interaction of photons of energies much above those available from artificial sources. The most that can be said about the variation of photo-nuclear cross-section with energy at the moment is that there is no strong evidence to suggest a cross-section varying very much from 10^{-28} cm.^{2}/nucleon between 1 and 40 GeV.

The last session was devoted to a discussion of the results of recent experiments on low-energy muons and electrons. The general impression that emerges from studies of muon decay and capture is that whereas the decay process is fairly well understood there are still some uncertainties in the explanation of the observed capture-rates. The discussion of electron interactions centred mainly around the Stanford work on nuclear sizes. One of the most interesting results of this work is the small size of the electrostatic charge core of the neutron. The interpretation of this result is not clear and the confirmation or otherwise of this result by more accurate experiments is awaited.

The conclusions to be drawn from this rather overworked Conference appear to be that there is still much to be learned about virtually every aspect of the subject. It would appear that for some time to come cosmic ray experiments are likely to be the only source of knowledge on nuclear processes at energies greater than 20 GeV. A. W. WOLFENDALE

COMMONWEALTH UNIVERSITIES' CONGRESS, 1958

THE Eighth Quinquennial Congress of the Universities of the Commonwealth, the first to be held outside the United Kingdom, was held in Montreal during the first five days of September. The Congress had been preceded by a smaller conference of executive heads of the Commonwealth Universities, held in the University of Toronto during the previous week. At that conference, some useful exchanges of view took place on some current university problems. The Montreal Congress was attended by more than 400 delegates and guests, many of them accompanied by their wives. Among the guests were some twenty-four American university presidents and the members of the administrative board of the International Association of Universities. The Congress was probably the most comprehensive gathering of representatives of the university world of the British Commonwealth and the United States which has yet taken place. There was consensus of opinion that never before had so much mutual understanding been achieved, both by the sessions of the Congress and otherwise, of the general and detailed patterns of university institutions in the countries represented at the Congress. Most of the Congress sessions were held at McGill University, although one session was held in the University of Montreal. Both universities provided accommodation and lavish hospitality for the delegates and their wives.

At the opening ceremony on September 1, the delegates and guests were welcomed by Dr. Andrew Stewart, president of the University of Alberta, in his dual capacities of chairman of the Association of Universities of the British Commonwealth and president of the National Conference of Canadian Universities. The Congress was formally opened by the Right Hon. Vincent Massey, governor-general of Canada, who warned that universities to-day tread a dangerous path in increasingly accepting government money, offered because they are doing things that government wants done. "The intellectual duty of the university to remain free is," he insisted, "greater now than ever, and more difficult than ever before." The opening address of the Congress, on "Expanding Education", was then delivered by Sir Hector Hetherington, principal of the University of Glasgow, who described himself as the veteran who had attended all but one of the previous seven congresses. He referred to two new elements in the expansion of university education in all the countries represented at the Congress—that the required rate of expansion is abnormally high, and that what is wanted is not a general all-round expansion but one designed to take effect mainly in one direction, science and applied science. Sir Hector posed no new problems and proffered no new solutions. He explained how the present situation had come about and what steps had been taken, and were being taken, to deal with it. He propounded the principles which, in his view, needed to be kept in mind in the expansion of professional education, if it were not to become mere vocational training, and he urged the value of keeping the humanities, together with science, at the centre of the university stage.

The first ordinary session of the Congress, on September 2, was devoted to a discussion of "Who should govern University Policy?" In this and subsequent sessions the speakers tended to outline the procedures and philosophies applicable to their own countries, and this brought to light rather unexpected degrees of divergence but there was very little attempt at synthesis; and the Congress formulated no general conclusions. The first speaker, Dr. V. C. Fowke (Saskatchewan), was concerned primarily with internal controls over university policy, and dealt specifically with the Canadian universities. He directed attention to two diametrically opposed concepts of university government: one, that a university ought to be a self-governing community of scholars, and the other, that it is a business enterprise which is best governed by typically corporation methods. The written constitutions of the Canadian universities tend strongly towards the latter. The allocation of funds, the determination of priorities and the selection of personnel are all the responsibilities of lay boards which have no academic representation. Usage, however, makes wide concessions to self-government and it is the academic staff who determine whom they shall teach and how they shall teach, with control of examinations. They cannot have these controls without an effective voice in financial allocations. Chancellor L. A. Kimpton (Chicago), the second opening speaker, elected to defend the American practice of giving the university administrator more power, perhaps more dignity, than is usually accorded him in the British tradition. He pointed out that most lay boards in the American universities have only fiscal interest and power, and he claimed that the administrator should have an important role in determining policy because of the inherent

limitations of the faculty. The defence of academic freedom is a matter to be undertaken by the university president, whose task will be the education of the public. Other functions of the president, in Dr. Kimpton's view, are: (*a*) the protection of the academic community from pressures which might make the university unbalanced; (*b*) to take strong remedial action with an inefficient or incompetent department, and (*c*) the raising of funds. None of these functions can be exercised effectively by academic bodies. In the ensuing discussion, Dr. T. Alty (Rhodes University, South Africa), doubted whether the principal or vice-chancellor of a Commonwealth university had functions very different from those of the American university president. He is a key figure and must exercise an important influence on university policy. Interpretation of the university to the public is not a function of the academic staff, and is best done by members of a lay governing body. But the determination of policy should be a co-operative enterprise; academic bodies, lay boards and university president all taking a share. Sir Keith Murray (University Grants Committee), while believing in self-government, stressed the need for lay participation, in which he saw four major advantages. The lay members can bring to the university the advantages of 'corporation' methods, they can exercise a semi-judicial function and help to solve otherwise insoluble problems, they can lighten the administrative load of the academic members, and they can help to promote public confidence, especially important as universities become increasingly dependent on public funds. Other contributions were made by Sir Charles Morris (Leeds), who agreed about the value of the lay members, but thought that the modern university should give the head of an academic department an important share in policy-making; by Prof. N. K. Sidhanta (Calcutta), who directed attention to the special problems of the 35 Indian universities, with some 800,000 students, of whom more than 700,000 were taught in the numerous affiliated colleges; and by Mr. A. Hakim (East Pakistan), Prof. K. E. Bullen (Sydney), Dr. C. H. Rautenbach (Pretoria), Prof. D. V. Cowen (Cape Town), President Grayson Kirk (Columbia), Mr. W. H. Gillespie (Canterbury Agricultural College), and Dr. H. B. Thom (Stellenbosch), who discussed the respective functions of the principal, the academic staff and the lay members in the determination of policy. There was a general appreciation of the valuable role of the lay member.

At the second session of the Congress Prof. J. F. Baker (Cambridge) opened a discussion on "Engineering Education, and its Place in the University". He gave a general survey of the engineering tripos course at Cambridge, an unspecialized course covering all the main branches of engineering science conducted in a single department of engineering. His satisfaction with the arrangements was not shared by President G. P. Harnwell (Pennsylvania) in respect of engineering education in the United States. Engineering was a latecomer among the academic disciplines; the lack of differentiation between professionalism and technicianism had operated to its disadvantage, and had hindered its recognition. Moreover, the greater emoluments and prestige of the practising engineer had adversely affected recruitment of academic staff. He thought that the closest possible association of engineering education with the universities should be maintained, and was unimpressed by the Soviet system of professional education in specialized institutes. President L. A. DuBridge (California Institute of Technology) asked where else than in the university would one have engineering education, and subsequent speakers were almost unanimously in agreement, giving various reasons, such as the close affinity with other sciences, the liberalizing influence of a background of other academic disciplines and, conversely, the beneficial influence of a faculty of engineering on other faculties. A discordant note was sounded by Dr. B. V. Bowden (Manchester College of Science and Technology), who pointed out that the industrial revolution was largely due to men who had never been to a university. He directed attention to the dual system of engineering education in the United Kingdom (in university and college of technology), and developed the doctrine that engineering is not only a mathematical science but also an art, with design playing an important part in the work of the engineer. Mr. A. Hakim (East Pakistan) referred to the difficulty of staff recruitment, and made a plea which was echoed by other Asian speakers in other sessions, for Western assistance, by a scheme of secondment or otherwise.

The complementary theme of "Medical Education and its Place in the University" was discussed at the session on September 3. The opening speaker was Lord Adrian (Cambridge), who reminded the delegates that medical schools have often grown up out of contact with universities, and that medical students have their hospital work to prevent them from becoming too narrow-minded. He suggested that segregation in the pre-clinical period could be lessened by giving more emphasis to general scientific training which could be shared with other students. Dr. F. G. Soper (Otago) and Sir Nicholas Attygalle (Ceylon) both saw great advantage in the intermingling of medical students and those of other faculties. Dr. Soper thought it even more important that the staff should intermingle. Sir David Campbell (Aberdeen) challenged the view sometimes held that the medical curriculum is entirely vocational, and suggested that medicine is in fact the most humanizing training available in a university. The university would be much the poorer if the medical faculty were removed. His views were supported by most subsequent speakers, representing opinion in Australia, Canada, India, Malaya, Nigeria and the United Kingdom. Various aspects of the medical curriculum were discussed, and it was suggested that postgraduate studies tend to be neglected.

At a private session on September 4 the Congress discussed some current problems in Commonwealth universities, especially those in Canada, New Zealand and South Africa. The final session, on September 5, was concerned with "The Establishment of New Universities". Dr. D. W. Logan (London) outlined the part which had been played by the external degree system of the University of London in the development of the new British university institutions, both at home and in the underdeveloped parts of the Commonwealth. He directed attention to the merits and defects of the system, which he thought was unlikely to continue as the normal procedure. The principal safeguards of the quality of work in new institutions would be the external oversight of appointments and examinations. President J. L. Morrill (Minnesota) pointed out that although both Canada and the United States derived their heritage of higher learning from the British universities, the policies and procedures for the establishment of new universities in both countries represented a marked departure from the British precedents. Both nations

had responded rapidly to the indigenous educational demands of fast-growing frontier societies and populations. "Universities are at once the catalysts and creations of a changing society." Several speakers agreed with Dr. Logan about the need in present circumstances to establish new universities. An impressive account of the principles adopted in the institution and development of seven new university institutions in the British Colonies was given by Dr. W. Adams (Rhodesia and Nyasaland). Lord Sinclair (Bristol) thought that the ultimate success of the Rhodesian experiment was of great importance to the whole British Commonwealth. Dr. C. H. Wilson (Leicester) stressed that two conditions were needed to warrant the foundation of new universities —local initiative and support, and a demand from prospective students. Dr. R. B. Madgwick (New England, N.S.W.) emphasized the weaknesses of a system of tutelage by existing universities. Dr. T. M. Advani (Bombay) referred to the remarkable demand for education in India after independence. The desire for knowledge is great, but the desire for acquiring degrees even greater. In referring to the service which universities provide for the community the Hon. P. M. Sherlock (West Indies) pointed out that the university may become a powerful competitor for limited resources. Dr. N. A. Mackenzie (British Columbia) asked whether, when it is difficult to obtain staff of adequate quality for existing institutions, it is wise to found new ones, and Dr. V. K. R. V. Rao (Delhi), after pleading for a national organization to lay down the principles on which a new institution should be established, asked: "What is a university?" At this stage these questions proved too difficult, and the Congress disbanded.

After the Congress, executive heads of Commonwealth universities and their wives paid a week-end visit to Washington and Philadelphia as guests of the Association of American Universities. In Washington they had the honour of being received by President Eisenhower at the White House, and of being addressed by Mr. Justice Frankfurter in the Supreme Court. The other delegates were entertained by Laval University in Quebec City. After the week-end, most of the delegates set off on one or other of eleven tours for which the transport costs were provided by a generous grant from the Carnegie Corporation of New York. Members of each party were thus enabled to visit some four or five universities in Canada and the United States, hospitality being provided by the universities concerned. For many of the delegates this was the most stimulating and rewarding part of their mission, as it allowed more intimate personal contacts than had been possible at the large Congress and gave a revealing insight into the workings of a variety of university institutions in the New World.

J. W. Cook

THE WORLD LAND USE SURVEY

THE World Land Use Survey owes its inspiration very largely to Prof. L. Dudley Stamp and his great achievement in carrying through in pre-war days the work and organization of the Land Utilisation Survey of Britain. A Commission, appointed at the International Geographical Congress held at Lisbon in 1949, was very impressed by the urgency of the problems of world population and world food supply and considered that "present factual knowledge is inadequate to serve as a proper foundation for schemes of improvement and development, especially in those areas which are commonly regarded as 'underdeveloped'". It proposed, therefore, a World Land Use Survey that would record the present use of land in all parts of the world on a uniform system of classification and notation, basing the maps on field-work together with the interpretation of other material such as air photographs. It hoped that a series of maps on the scale of 1 : 1,000,000 might be published together with explanatory memoirs that would help in the understanding of the maps.

The work in different parts of the world has met with varying success. Some pilot surveys suggested that, elaborate though the land-use classification was, it often required further amplification, and sometimes modification. Aspects of the work have been taken up by Government departments, such as the Directorate of Overseas Surveys which has developed most usefully the interpretation of air photographs as a source of land-use data.

Some preliminary results are becoming available through the issuing of maps and reports. A map of Cyprus at a scale of 1 : 250,000 was published in 1956[1]. It was based on the stereoscopic examination of 10,000 photographs and was prepared in the Department of Geography at the London School of Economics under the direction of R. R. Rawson and K. R. Sealy. The first of the Survey's 'Occasional Papers', "Land Use Studies in the Transvaal Lowland", by Dr. Monica M. Cole, of the University College of North Staffordshire and formerly of the University of the Witwatersrand, also appeared in 1956[2]. It was a "contribution to the study of the opportunities and difficulties inherent in the savannah environment" and laid emphasis upon the many environmental factors that challenged the area's agricultural development.

Recently, the Survey has published the first of its Regional Monographs, "A Survey of Land Use in Hong Kong and the New Territories", by Dr. Thomas R. Tregear, lecturer in geography in the University of Hong Kong[3]. The volume includes a coloured land-use map at a scale of 1 : 80,000 distinguishing eight types of land use: woodland, scrub, rough grassland, 'badlands' that are heavily eroded, arable, swamp, houses with gardens, and built-up areas, including camps, cemeteries and other land that is agriculturally unproductive. Hong Kong illustrates in a special way the necessity for the fullest possible use of such land as is available, with its great population (estimated at between 2 and 2½ millions and increasing at more than 70,000 per annum) crowded into a mere 400 square miles of the Earth's surface. There is the sharp contrast between the crowded urban areas of Hong Kong and Kowloon and the rural districts of the New Territories. Serious problems arise from the mountainous nature of much of the area and from the heavy, often torrential, rainfall which is largely responsible for the soil erosion that has created the 'badlands' of the open hillsides.

Dr. Tregear has tried to bring together the basic data necessary for the use of planners and administrators, and to indicate the sources from which fuller information can be obtained. His is a factual survey, a record of things as they are, not a forecast of possible developments nor a catalogue of suggested remedies for the territory's land-use problems. This is exactly as it should be and it is indeed the justification for all land-use surveys. They may be difficult to carry out and they may sometimes seem very wasteful of time and energy; yet without them there can be no precise and objective assessment of land use as it can be observed to-day. Subjective judgments, wishful thinking and intelligent anticipation are all specifically excluded from the purpose of the World Land Use Survey.

In essence, Dr. Tregear's monograph is an exposition and elaboration of the land-use map prepared. At times the literary style is weak, and occasionally the text becomes little more than a series of notes. A few of the diagrams are disappointing because they cannot be read easily or have been excessively reduced. Sometimes Dr. Tregear might have emphasized more those relationships of physical and human phenomena that geographers claim as a special part of their field. There may well be monographs with a rather more penetrating analysis later in this series. Nevertheless, the volume deserves a welcome by geographers and others both for its own worth and as an indication of what may be expected for other areas in the future. It is a sign that the World Land Use Survey has passed beyond the talking and planning stages and, in some countries at least, beyond the field-work to the point where maps and reports are being produced. Clearly the editor, Prof. Stamp, who has just retired from his chair in the University of London, is going to be as active as ever in the years to come. We can, therefore, anticipate a series of regional monographs for the world that will be comparable in conception, content and importance to the well-known County Reports of the Land Utilisation Survey of Britain.

Robert W. Steel

[1] Rawson, R. R., and Sealy, K. R., "Land Use Map of Cyprus": 35 in. × 22 in. (Bude: Geographical Publications, Ltd., 1956.) 3s.

[2] Cole, M. M., "Land Use Studies in the Transvaal Lowland" (World Land Use Survey: Occasional Paper 1). Pp. 41+37 figs. (Bude: Geographical Publications, Ltd., 1956.) 5s.

[3] Tregear, T. R., "A Survey of Land Use in Hong Kong and the New Territories". (The World Land Use Survey: Monograph 1.) Pp. v+75+1 map. (Hong Kong: Hong Kong University Press; Bude: Geographical Publications, Ltd., 1958. Distributed outside Hong Kong by Macmillan and Co., Ltd.) 12s. 6d.

THE FRESHWATER BIOLOGICAL ASSOCIATION

BESIDES details of the administration, organization and state of the finances of the Freshwater Biological Association for 1957–58, the twenty-sixth annual report contains a statement by the Director on the scientific work of the staff.

In the chemistry section analyses of algae have shown that cobalt, copper and zinc are present in the plant tissues in amounts the ratios of which are similar to those of their concentrations in the environment, a fact which suggests that the uptake of such elements by algae may be governed rather by their concentrations in the surrounding water than by any physiological needs of the plant.

Earlier work on the acid waters of blanket bogs in the Pennines and of bog lakes in Nova Scotia suggested that both owed their acidity to sulphuric acid. Dr. E. Graham has now extended these studies to bog waters elsewhere in Britain and in less-oceanic sites in Poland with similar results. Since sulphuric acid also seems to cause the acidity of the soil solutions extracted from heavily leached mor humus layers overlying podzolic soils in Lake District oak woods, it is probably to be regarded as an important agent in soil leaching. While in Britain it comes largely from atmospheric pollution brought down in rain, there is evidence that it is also produced by the breakdown of organic sulphur compounds in the soil; it may therefore be important in unpolluted areas also.

Continuing his observations on the fluctuations in numbers of the smaller nannoplankton, Dr. J. W. G. Lund finds a clear difference between the periodicity of the very small green algae in the surface waters of Windermere, Esthwaite Water and Blelham Tarn and that of the larger species. Thus, large populations of the small forms have been observed in late winter and early spring. It will, however, be necessary to continue observations over several years to determine whether this happens regularly.

Work on the polycentric chytrids which occur in the reed beds of Windermere has been continued by Dr. L. G. Willoughby, who is making a comparative study of eight isolates of *Cladochytrium replicatum*. So far, particular attention has been paid to growth-rates and fruiting (that is, zoosporangium formation) on agar. One of the isolates has been uniformly sterile under all conditions, while another has only rarely formed zoosporangia. Two further isolates of the eight can be segregated not only on purely morphological grounds, but also because the rate of linear growth on agar is consistently high. The effect of light on growth and fruiting in this fungus has been investigated. Light is not essential for pigment and hence zoosporangium formation, and total growth, as measured by the increase in colony diameter on agar, is independent of this factor. It seems clear, however, that fruiting is generally greater in light than in the dark, the effect being particularly noticeable in the isolates with high fruiting capacities.

A further study has been made of the influence of the container on the rate at which bacteria multiply in samples of lake water stored in the laboratory. This has been extended to cover polyethylene and nylon containers as well as those of silica, 'Pyrex' and soda-glass. The conclusion reached previously that silica provided the least 'active' surface for bacterial growth was confirmed; the others follow in the order 'Pyrex', soda-glass, polyethylene up to nylon, which stimulates the largest bacterial growths. It appears that the surface properties of polyethylene and nylon in particular facilitate the supply of something the bacteria need, whereas silica has no such property, regardless of the type of water, the temperature, or of whether the containers are stationary or shaken. This is borne out by the discovery that in experiments using a constant circulation of water, considerable multiplication of bacteria took place wherever the

liquid remained in contact with polyethylene or nylon connecting tubes. These results may have direct practical importance on industrial process problems, where polyethylene pipes become blocked by masses of slime-forming bacteria attached to the walls, and in the storage of non-sterile solutions in containers made of these materials.

The use of opercular bones to estimate the age and past growth of pike has been further investigated by Dr. Winifred Frost and Miss Charlotte Kipling, who concluded last year that growth can be calculated accurately by simple proportion from measurements of the annual rings, making an arbitrary choice by inspection of a centre from which to make the measurements. Since the rings near the centre are not always clearly visible, the method does not give reliable estimates of growth in the early years of life. This difficulty has been overcome by the use of theoretical growth-tables derived from Ford's growth formula, using data from Windermere calculated for slow-, medium-, fast- and very fast-growing fish for the two sexes separately. By comparing the growth in later years of any individual fish with these tables, it is usually possible to assign it to one of the growth-rate categories. This makes it possible to infer its true age and so to decide whether the first discernible ring represents its first, second or third winter.

D. F. Westlake has measured the rate of production of oxygen by *Ranunculus* spp. in a closed, static system, at various light intensities. The highest gross rate of oxygen production found for light-saturated plants was about 10 mgm. of oxygen hr./gm. (dry weight) at 15° C. Light-saturation was approached at 10,000 lux, and both this and the maximum rate of oxygen production are lower than generally reported in the literature on higher plants. Possibly this is the result of using static conditions for the experiments, and apparatus for determining oxygen production in flowing conditions is being developed.

MECHANICAL ENGINEERING RESEARCH LABORATORY

REPORT FOR 1957

THE report on the work of the Mechanical Engineering Research Laboratory for 1957* makes fascinating reading, and contains much that will interest any engineer and many physicists.

The chairman of the Engineering Research Board directs attention in his report to the difficulty of getting the results of the Laboratory's work both disseminated and applied. Most engineering scientists have yet to learn that a paper which may lead in due course to scientific honour is unlikely to be understood by many practising engineers, however high their theoretical attainments; the work must also be published as a straightforward physical description, written in lucid English and devoid of mathematics if it is to be read and applied. Sir Charles Inglis used to state this truth regularly in his lectures; few have learned the lesson.

The proportion of scientific and experimental staff is 160 out of a total of 444. This seems high. Does the Laboratory suffer from the difficulty common in Government and university laboratories of being hamstrung financially in providing adequate ancillary and office staff?

In recommending a rapid expansion of the Laboratory, the problem of how it, the universities and the colleges of advanced technology are all to be staffed must arise. In Germany, most of the work similar to that done at the Mechanical Engineering Research Laboratory is done in institutes of the Technische Hochschulen. Might it not be better to give the colleges of advanced technology similar institutes?

While it is clear why some of the research, both fundamental and applied, is being done nationally, it is surprising to find that fundamental work on greases has not already been undertaken on an adequate scale by private industry. When such gaps are found, is it not desirable that they should be investigated where the staff concerned can also be available for part-time teaching?

Nevertheless, the report describes the development of fine facilities and the accomplishment of much excellent work. Many firms should read it and send members of their staff to see what is being done.

D. B. WELBOURN

* Department of Scientific and Industrial Research. Mechanical Engineering Research 1957: Report of the Mechanical Engineering Research Board, with the Report of the Director of Mechanical Engineering Research. Pp. iv+63+4 plates. (London: H.M. Stationery Office, 1958.) 4*s.* 6*d.* net.

TILT CRITERIA AND DIRECTION OF ROTATION OF SPIRAL GALAXIES

G. DE VAUCOULEURS has a paper with the above title in the *Astrophysical Journal*, **127**, 2; March 1958, in which he presents a review of the observational evidence on the direction of rotation of the spiral pattern in ordinary and barred spirals. A growing body of evidence suggests that the formation of spiral structure is governed by the large-scale magnetic and hydrodynamical properties of the interstellar medium in rotating galaxies, and according to current ideas, dust or 'smoke' particles may form out of the gaseous medium and induce the condensation of gas clouds into stars or groups of stars. The author of the paper has discussed the morphology of spiral structure and its bearing on the large-scale instantaneous distribution of gas and dust in galaxies (*Hand. Phys.*, 53), and in the present paper he deals with the systematic motion of the interstellar substratum on the largest scale in a galaxy, in other words, with the general rotation of the spiral pattern. The previous investigations of those who have devoted their attention to this subject—Baade, Hubble, Lindblad, Stebbins, Zwicky and others—are referred to, and the reasons for the divergences in the interpretations are analysed. The discussion is recapitulated in Table 1, p. 499, which consists of eleven columns (the symbols used in these are explained at the end of the table and also on the previous page) and the conclusions are briefly as follows.

Comparing this table with similar tables of Hubble published in 1943 it appears that of the fifteen objects in his Table 1, "Well Observed Nebulæ", six are in common with the present discussion, and the conclusion that the arms are trailing in the rotation appears unequivocally confirmed by one or several of the primary or secondary criteria. Of the eight objects in Hubble's Table II, "Doubtful Cases", five are in common and three have been removed from the doubtful class by the application of one or several of the same criteria. *NGC* 5005, which was doubtful only in respect to the sense of spectroscopic rotation given by Slipher, has now been confirmed by Mayall, and the last one (*NGC* 4594) is indecisive. It is pointed out in Appendix I, however, that in 1951 Lindblad attempted to unravel the direction of its spiral pattern by means of a geometric restoration in the plane of the spiral of the distribution of bright knots measured on a photograph in ultra-violet light with the 200-in. reflector. Fig. 9*a*—Lindblad's interpretation—is not unambiguous, and an alternative interpretation (*b*) of the distribution appears at least as plausible, and this leads to the opposite direction for the spiral pattern and hence to 'trailing' arms. From additional evidence which is given it seems clear that although *NGC* 4594 is not a decisive case, nevertheless the available evidence favours interpretation *b* rather than *a*.

NGC 5746, Fig. 10, as pointed out in Appendix II, is a "true spindle" with a class 1 obscuration pattern similar to *NGC* 4594, and there is no doubt as to which is the near side. In 1917 Pease described the direction of the spiral pattern as "right-handed" from the evidence of a fair plate with the 60-in. reflector, and in 1943 Hubble independently concluded that "the pattern is right-handed, on the basis of good plates with the 100-in. telescope". He admitted, however, that the arms were difficult to trace and decided to include it with the doubtful cases. Pease and Hubble's conclusion is substantiated from the evidence of a good blue plate taken with the 200-in. reflector and shown in Fig. 3, and this is made obvious by a restoration of the bright and dark arms in the plane of the spiral, as shown in Fig. 10.

VISUAL PIGMENTS OF THE OCTOPUS AND CUTTLEFISH

By PAUL K. BROWN and PATRICIA S. BROWN

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THE first molluscan visual system to be examined chemically was that of the common squid, *Loligo pealii*. This animal possesses a rhodopsin comparable with that found in vertebrate rods, composed of neo-b retinene joined to the protein, opsin[1,2]; but under physiological conditions, squid rhodopsin engages in a more limited series of reactions than occur in the vertebrate retina. In vertebrate rods, rhodopsin bleaches in the light, over the transient intermediates lumi- and meta-rhodopsin, to a mixture of retinene and opsin; then retinene is reduced to vitamin A. In the squid retina, the little vitamin A that is present seems to take no immediate part in the visual processes[3]; and light does not normally bleach rhodopsin, but converts it to metarhodopsin. Vertebrate metarhodopsin is highly unstable, hydrolysing rapidly to retinene and opsin; but squid metarhodopsin is stable, the retinene remaining attached as chromophore to opsin. The change from rhodopsin to metarhodopsin involves only the isomerization by light of the chromophore retinene from the neo-b configuration (11-*cis*) to all-*trans*. Light also causes the reverse isomerization, from all-*trans* to neo-b. That is, in the squid retina light brings into a steady state the system:

$$\text{rhodopsin} \underset{\rightleftharpoons}{\overset{\text{light}}{}} \text{metarhodopsin (ref. 2)}$$

This pair of reactions, which only introduces the rhodopsin system in a vertebrate, is the entire system of the squid.

A period spent at the Stazione Zoologica in Naples afforded us an opportunity of working on the visual systems of the octopus (*Octopus vulgaris*) and cuttlefish (*Sepia officinalis*). The animals were dark-adapted 8–10 hr., and the retinas dissected out under red light, and frozen. After thawing, the tissue was ground in a cold mortar in 40 per cent sucrose (w/v). The suspension of tissue in a centrifuge tube was covered with a layer of neutral phosphate buffer, and centrifuged at 20,000 r.p.m. The rhabdomes or 'rods' collected in the interface between sugar solution and buffer, and were drawn off with a syringe. The residual tissue was re-ground in 40 per cent sucrose as before, and re-layered in the centrifuge. The suspensions of rods from both layers were combined, diluted with neutral buffer, and the rods were sedimented in the centrifuge. They were re-suspended in cold 35 per cent sucrose, covered with a layer of buffer, re-centrifuged, and again collected from the interface. The rod sediment was stirred into a large volume of 1 *M* disodium hydrogen phosphate (*p*H 8), and again collected by centrifuging. These repeated fractionations and washings were performed to remove extraneous pigments. The final washings were colourless. Finally, the rods were extracted with 1 ml. of 2 per cent digitonin solution. The yields of these procedures were: rods from 6 octopus in 1·0 ml., $E_{max.}$ 0·38; rods from 4 *Sepia* in 1·0 ml., $E_{max.}$ 0·49. The retinae contain much more pigment than this; much material was wasted in the fractionations to achieve purity.

Both extracts were used in almost identical series of measurements. The results are shown in Figs. 1 and 2, and in Table 1.

Table 1

	Octopus vulgaris		*Sepia officinalis*		*Loligo pealii*	
	$\lambda_{max.}$ (mμ)	Molar extinction (ε)	$\lambda_{max.}$ (mμ)	Molar extinction (ε)	$\lambda_{max.}$ (mμ)	Molar extinction (ε)
Rhodopsin	475	37,000	492	37,000	493	40,600
Alkaline metarhodopsin	380	56,200	380	54,500	380	60,900
Acid metarhodopsin	503	44,400	497	47,700	500	59,700
Alkaline indicator yellow	369	55,500	367	48,400		
Acid indicator yellow	443	44,400	443	42,200		

The absorption spectrum of *Sepia* rhodopsin is like that of *Loligo*, with $\lambda_{max.}$ 492 mμ. *Octopus* rhodopsin lies at much shorter wave-lengths, with $\lambda_{max.}$ 475 mμ, and is orange rather than red in colour. In this regard it resembles the rhodopsins of deep sea fishes[4]. In both cephalopod rhodopsins a small β-band is present at about 360 mμ.

By exposure to light at *p*H 9 and 2° C., *Sepia* and *Octopus* rhodopsins were converted to the corresponding metarhodopsins. The spectra of these substances, measured at *p*H 9, 7 and 5, showed that they are *p*H indicators, as in *Loligo*[2]. In alkaline solution, the metarhodopsins of all three organisms have $\lambda_{max.}$ about 380 mμ. In acid solution these substances become highly coloured, apparently through adding a proton; $\lambda_{max.}$ of the acid metarhodopsins are a little different in each organism (Table 1). These changes are wholly reversible. The absorption spectra at all three *p*H's exhibit a common or isosbestic point, showing that they represent stoichiometric interconversions between a specific initial and a specific final state. This appears to involve, as in *Loligo*, the equilibrium:

$$\text{metarhodopsin} + H^+ \rightleftharpoons \text{metarhodopsin}-H^+$$

In all these cephalopods of the $\lambda_{max.}$ of acid metarhodopsin lies at longer wave-lengths than that of rhodopsin, and its extinction is also higher. As a result, on exposing these rhodopsins to light, they deepen in colour rather than bleach. *Octopus* presents the extreme of this condition; the $\lambda_{max.}$ of its metarhodopsin is 28 mμ longer than that of rhodopsin, so that when *Octopus* rhodopsin is irradiated it changes in colour from orange to red.

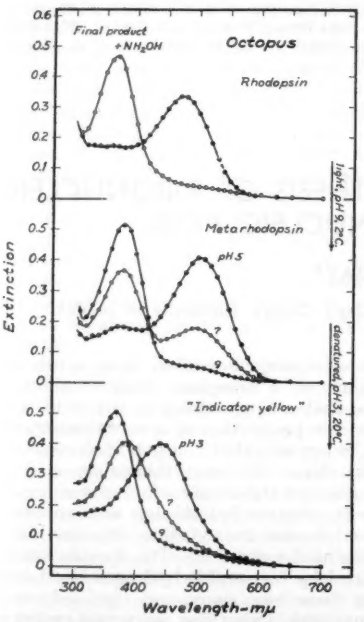

Fig. 1. Visual pigments of the octopus. Top, right: rhodopsin, $\lambda_{max.}$ 475 mμ. Middle row: metarhodopsin, formed by irradiating rhodopsin. This is a *p*H indicator, going reversibly between an alkaline form ($\lambda_{max.}$ 380 mμ) and an acid form ($\lambda_{max.}$ 503 mμ), both with a higher extinction than rhodopsin. Bottom row: the metarhodopsin has been converted to 'indicator yellow' by denaturing with acid. This changes in colour with *p*H, going from a protonated Schiff base in acid solution ($\lambda_{max.}$ 443 mμ) to a mixture of free retinene and denatured opsin in neutral solution ($\lambda_{max.}$ 385 mμ), and to an indiscriminate mixture of Schiff base linkages between retinene and opsin in alkaline solution ($\lambda_{max.}$ 369 mμ). At the end of these procedures, the product was treated with hydroxylamine to convert all retinene to retinene oxime; the resulting spectrum is shown at the top, left

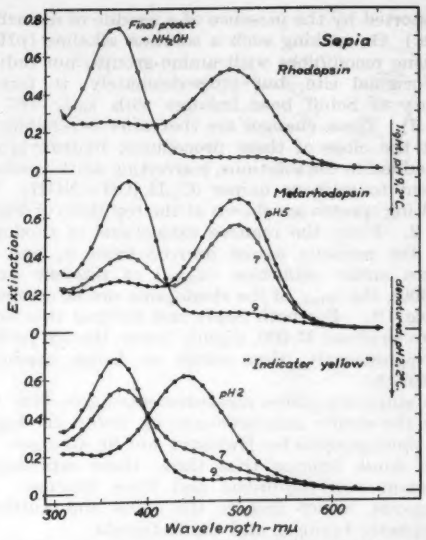

Fig. 2. Visual pigment of the cuttlefish. Top, right: rhodopsin ($\lambda_{max.}$ 492 mμ). Middle row: metarhodopsin at *p*H 5, 7 and 9. Bottom row: 'indicator yellow' at *p*H 2, 7 and 9. In this instance it appears that the acid denaturation of metarhodopsin was not wholly completed, and this accounts for some distortion of the spectra of indicator yellow, particularly at *p*H 7. The appearance of a common or isosbestic point in the spectra of indicator yellow is also a fortuitous result of this distortion. At the end of these procedures the product was treated with hydroxylamine to convert retinene to retinene oxime; the resulting spectrum is shown at the top, left

In rhodopsin the aldehyde group of retinene appears to be combined with a specific amino-group of opsin in a Schiff base linkage:

$$C_{19}H_{27}CHO + H_2N\text{–opsin} \rightarrow C_{19}H_{27}CH{=}N\text{–opsin} + H_2O$$

To explain the colour, it is assumed that this has added a proton, the charge of which induces a greatly increased resonance in the conjugated system of retinene: $C_{19}H_{27}CH{=}NH^+$–opsin; and supposes also that a close steric fit between the hydrocarbon portion of the retinene molecule and the protein, permitting a high degree of interaction between the two, further enhances the resonance[6]. In metarhodopsin (acid form), much the same situation obtains, except that retinene has gone from the neo-b to the all-*trans* configuration; this also appears to be a protonated Schiff base, its spectrum still enhanced by the steric fit between retinene and opsin[2].

The metarhodopsins were now denatured by being brought to a high acidity (*p*H 2–3). We shall call this product 'indicator yellow'. With the denaturation of opsin, the fit between it and all-*trans* retinene is lost, with a corresponding loss of colour. The $\lambda_{max.}$ falls to 443 mμ, the position found in a variety of model Schiff bases of retinene when acidified[7]. The retinene is probably still attached to the original amino-group (the "N-retinylidene opsin" of Morton and Pitt, yet with denatured opsin); but on neutralization of the solution, it hydrolyses off, to yield free retinene and denatured opsin[8]. The $\lambda_{max.}$ of these preparations, brought to *p*H 7, is therefore that of free retinene, about 385 mμ. (In Fig. 2 this spectrum

is distorted by the presence of a residue of metarhodopsin.) On making such a solution alkaline (*p*H 9), retinene recombines with amino-groups, not only at the original site, but indiscriminately, to form a variety of Schiff base linkages with $\lambda_{max.}$ 367 mμ (ref. 7). These changes are thereafter reversible.

At the close of these procedures, hydroxylamine was added to the solutions, converting all the retinene present to retinene oxime ($C_{19}H_{27}CH{=}NOH$). The resulting spectra are shown at the top (left) of Figs. 1 and 2. From the relative extinctions of rhodopsin and the retinene oxime derived from it, and the known molar extinction ($\varepsilon_{max.}$) of retinene oxime (51,600), the $\varepsilon_{max.}$ of the rhodopsins can be computed (Table 1)[9]. For both *Sepia* and *Octopus* this comes out to be about 37,000, slightly lower, though perhaps not significantly, than cattle or *Loligo* rhodopsin (40,600)[9].

In summary, these measurements agree very well with the earlier measurements on *Loligo* rhodopsin, and their analysis by Hubbard and St. George[2]. It is of some interest that these three cephalopods represent two sub-orders and three families: the Decapoda, which include the squid and cuttlefish in separate families, and the Octopoda.

The rhodopsins of these cephalopods demonstrate a condition that has already become familiar in vertebrate rhodopsins: a considerable spread of absorption spectra, $\lambda_{max.}$ ranging from 475 to 493 mμ. In these animals as in the vertebrates this variation results from the fact that though all known rhodopsins have the same chromophore, neo-b retinene, each species of animal possesses a different opsin; and with this go differences in the absorption spectrum and other properties.

In all three cephalopods, the action of light on rhodopsin yields a relatively stable metarhodopsin, which probably changes no further under physiological conditions. It was realized some time ago that, even in vertebrates, visual excitation cannot wait upon the relatively slow process of bleaching—the release of retinene—but must depend upon the initial reactions, the formation of lumi- and metarhodopsin[10]. In the cephalopods the visual system appears to involve no further degradation. In these animals, as in vertebrates, the visual pigments must be derived ultimately from vitamin A itself, but apparently by some—probably slow—side-reaction, not directly and continuously part of the visual cycle.

This investigation was supported in part by a grant to Prof. George Wald from the U.S. Office of Naval Research. We should like to thank Dr. Peter Dohrn, director of the Naples Zoological Station, and members of the staff for the facilities placed at our disposal there and for their many kindnesses during our stay.

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A TEMPLATE MODEL FOR THE SYNTHESIS OF RIBONUCLEIC ACID FROM DEOXYRIBONUCLEIC ACID

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THE suggestion has been made that the nucleotide composition of nuclear ribonucleic acid could be accounted for by assuming that the nuclear ribonucleic acid is synthesized on a double helical deoxyribonucleic acid template with each base pair providing a specific site for a nucleotide of ribonucleic acid[1]. The two alternative possibilities to which one is led by these chemical data are listed in Table 1, where *A–T* 1 refers to the deoxyribonucleic acid base pair with adenine on chain 1 of the double helix and thymine on chain 2, and *A–T* 2 to the reverse situation. If this scheme is correct, it might be possible to determine the actual sites on the template by examination of molecular models, and it is the purpose here to discuss the results of a systematic investigation of molecular models.

Initially, let us consider some of the general requirements of a template which we define as a system capable of producing a polymer with a specific linear sequence of monomers. We shall take the problem of deoxyribonucleic acid synthesis as an illustration of a template because there is good evidence that a single chain of this acid is the template for the production of a complementary chain[2]. That is, it appears that the polynucleotide surface of a single chain of deoxyribonucleic acid provides specific sites for the construction of a complementary chain with adenine functioning as a specific site for thymine, guanine for cytosine, thymine for adenine and cytosine for guanine. The specific site is partly determined by favourable hydrogen-bond interaction between these base pairs, but obviously more than this is involved. Otherwise, we would expect adenine, for example, to be a site for guanine as well as thymine, since it is possible for adenine to form the same pair of hydrogen-bonds with the latter two

Table 1

Deoxyribonucleic acid base pair (*a*)	Deoxyribonucleic acid base pair (*b*)	Ribonucleic acid base determined
A–T 1	or *A–T* 2	guanine
A–T 2	or *A–T* 1	cytosine
G–C 1	*G–C* 1	uracil
G–C 2	*G–C* 2	adenine

* Postdoctoral Research Fellow of the U.S. National Science Foundation.

nucleotides. We have concluded that the success of the deoxyribonucleic acid template is at least partly due to the fact that the hydrogen-bonded base pairs, adenine and thymine, guanine and cytosine, are identical in so far as they may be fitted into a completely regular double helix structure. If we visualize the process of polymerization involving the template the advantages of this structural regularity becomes clear. Consider a single chain of deoxyribonucleic acid acting as a template and a second growing chain partly formed on it; then, where a second chain is formed, the resulting double chain polynucleotide would probably coil up into a helical structure identical with deoxyribonucleic acid because this would be the energetically favourable situation. If we now add a monomer to the growing chain, and adenine is the first unpaired base on the template, either guanine or thymine could form the same pair of hydrogen-bonds with it. However, due to the deoxyribonucleic acid-like configuration of the polynucleotide chain to which we expect the monomer to add, only thymine can hydrogen-bond favourably with adenine and still have its reactive sugar phosphate group in a position where addition to the growing chain is possible (regardless of the intermediate chemical steps involved). Thus, only thymine is capable of becoming a permanent component in the growing polynucleotide chain when the opposing base on the template is adenine. A similar argument would apply to the other bases. In summary, we see that the specificity of the deoxyribonucleic acid template site (apart from enzymes involved) involves at least two conditions: (1) energetically favourable binding of its monomer nucleotide counterpart; (2) binding in such a way that the reactive group of the bound monomer is in a position to condense on the growing end of the polymer chain.

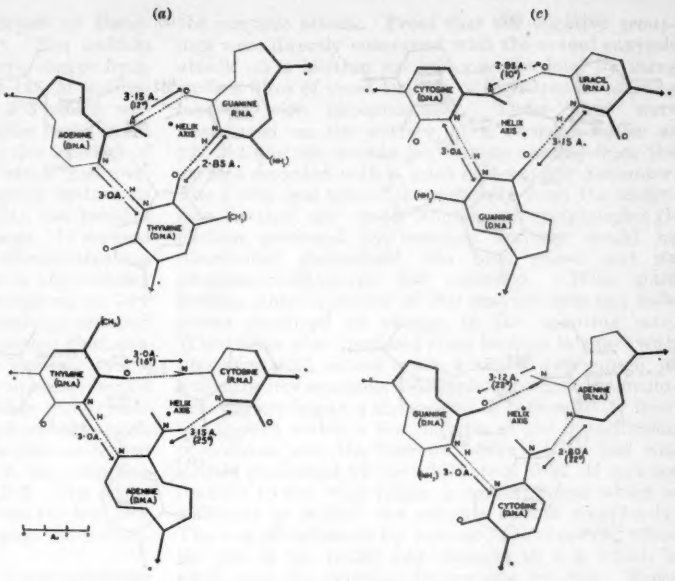

Fig. 1. Nucleotide triplets which may be involved in the template

I have attempted to find specific sites for the binding of the four commonly occurring ribonucleotides to the deoxyribonucleic acid base pairs which would satisfy requirements similar to the two just discussed. Initially, I sought specific sites for binding ribonucleotides to the deoxyribonucleic acid in its normal double helical configuration. However, it was not possible to satisfy conditions (1) and (2) simultaneously and, therefore, I have concluded that deoxyribonucleic acid is not capable of acting as a template for ribonucleic acid synthesis without undergoing major configurational changes. Indeed, only one type of modification in the deoxyribonucleic acid molecule has led to a molecular model in which we could approximately satisfy our two conditions. This modification involves three steps: the breakage of hydrogen-bonds between the amino-group and the carbonyl group in both base pairs of the deoxyribonucleic acid; the twisting of the planes of the bases relative to one another; and, in some cases, a rotation of the adenine and cytosine amino-groups out of the plane of the base. (A similar change has been described in more detail for the synthetic complex, polyadenylic acid/2 polyuridylic acid[3].) Together with these alterations in the bases, adjustments in the configuration of the sugar phosphate backbone becomes necessary; nevertheless, I shall leave these unspecified at present. The systematic breakage of the amino-carbonyl hydrogen-bonds leaves the two deoxyribonucleic acid chains still connected by NH . . . N hydrogen bonds. If we now consider the binding of ribonucleic acid base groups by this system, there are in all eight nucleotide triplets we must inspect. First, we have attempted to build identical hydrogen-bonded triplets (identical being used in the same sense as before) using the four triplets that would occur in the code suggested from the chemical data in Table 1. In Fig. 1 we see the outcome of this attempt. The base triplets are shown in two-dimensional projection. The bases are represented by light, medium and heavy lines to illustrate that they are respectively, below, in or above the plane of the paper. In all cases, the deoxyribonucleic acid base on chain 1 is drawn in the plane of the paper, and the other two bases are tilted from the plane of the paper by about 18°. The helix axis is perpendicular to the plane of the paper; its indicated position is only approximate. (I have arbitrarily chosen the tilting arrangement in the figures since it would be possible to tilt in the reverse fashion, by taking the mirror image in the plane of the paper. Probably when the problem of wrapping the triplets into a helical structure is considered in more detail, regular tilting of one sort would be favoured.) The arrows attached to the nucleotides represent the connecting link to the C_1 atoms of the sugar. The dots near these arrows represent the average positions of the C_1 atoms for the four triplets and it can be seen that the maximum deviation from this average is 0·5 A. The hydrogen-bond distances, N—H . . . *X*, are indicated in the figures, and the deviation of the N—H . . . *X* angles from linearity is indicated in

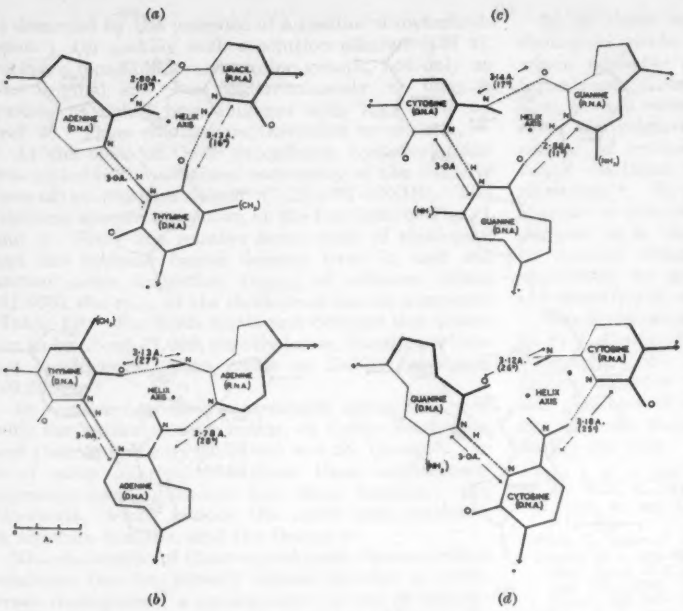

Fig. 2. Nucleotide triplets which might interfere with the template

parenthesis below the hydrogen-bond distances. I have used the limits suggested by Donohue[4] for the hydrogen-bond lengths and I have restricted the deviation of the N—H . . . X angle from linearity to 28°. Within these limits it has not been possible to make the four triplets identical. Nevertheless, it seems likely that it would be possible to construct a fairly regular three-stranded helical model with reasonable van der Waals contacts using the triplets in Fig. 1 more or less interchangeably. Thus, the template model suggested by Fig. 1 is structurally reasonable and consistent with the chemical data in Table 1. Consequently, a three-stranded helical molecule involving the triplets in Fig. 1 could be an intermediate complex in the synthesis of nuclear ribonucleic acid.

Despite this limited success with the model, there arises a serious difficulty concerning specificity. In each of the four triplets shown in Fig. 1, it is possible to substitute a different ribonucleotide to produce a hydrogen-bonded triplet with approximately the same dimensions. These alternative triplets are illustrated in Fig. 2 and their occurrence suggests that my template lacks specificity. If further investigation of complete three-dimensional molecular models does not lead to the exclusion of these alternative triplets we would be forced to conclude that the specificity of the template was partly determined by the ribonucleic acid polymerizing enzymes.

In conclusion, we see that even though the model-building investigation has not yielded a total solution to the problem of how deoxyribonucleic acid may act as a template for ribonucleic acid synthesis, it has narrowed down the possibilities we must consider. If, for example, the code suggested by the relative composition of the deoxyribonucleic acid and nuclear ribonucleic acid is correct, we can see from comparison of Fig. 1 with Table 1 that the model clearly limits us to alternative (*b*) in Table 1. I have only made a preliminary approach to the problem of building complete three-dimensional helical models because of the large number of possible sequences of nucleotide triplets, and an investigation of these possibilities will be postponed until more chemical data have been obtained.

I would like to thank my colleagues at this Laboratory for the use of molecular models and for their advice and criticism.

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CONTROL OF LECITHINASE ACTIVITY BY THE ELECTROPHORETIC CHARGE ON ITS SUBSTRATE SURFACE

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IT has been shown that a preparation of the phospholipase (lecithinase) from *Penicillium notatum* which normally only hydrolyses lyso-phospholipids will also attack lecithin providing this substrate contains small amounts of an activating lipid, such as monophosphoinositide or polyglycerolphospholipid[1]. The addition of these activating lipids to lecithin caused a marked reduction in the extent to which the lecithin was extracted from aqueous emulsions by lipid solvents such as ether, a property which ran closely parallel to the development of enzymic activity[2]. This suggested that the activation was connected with some change in the surface of the lecithin particles. It was, therefore, decided to examine the particles by microelectrophoresis so as to determine the sign and magnitude of their electrophoretic charge.

Ovolecithin was isolated by chromatography on alumina and silicic acid columns as described previously[3], and emulsions were examined in a micro-

electrophoresis cell of the type developed by Bangham, Flemans, Heard and Seaman[3]. The lecithin particles were found to have a net zero charge from *p*H 3·0 to 13·0 when emulsified in 0·145 *M* sodium chloride. In formate buffer at *p*H 3·3 which was optimal for enzyme activity, the particles had a small positive charge. On the addition to the lecithin of a small percentage of certain lipids which had previously been found to activate its enzymic hydrolysis (monophosphoinositide and cardiolipin), the lecithin particles acquired a net negative charge. It seemed likely that the reason for this was that these activating lipids possess a negative polar group in the tertiary dissociable hydrogen atom of the phosphate moiety which is not compensated for by a positively charged basic group. It was consequently expected that any molecules possessing a hydrophobic portion and a negatively charged polar group (amphipathic) would also render a lecithin surface susceptible to enzymic attack. It was shown that dicetylphosphoric acid, taurocholic acid and dodecyl sulphate also activated the enzyme system and produced a net negative charge on the lecithin surface at *p*H 3·3. The latter compound, however, would only activate the lecithinase within a comparatively narrow range of concentration.

With the activators so far studied, it was necessary to add a certain critical concentration to the lecithin before enzyme activity began. As the concentration of activator was further increased, the lecithinase activity rapidly reached a maximum, and with the further addition of activator there was a decrease in the amount of lecithin hydrolysed by the enzyme. At the concentration at which activation commenced, the lecithin had acquired a net negative electrophoretic charge which was approximately the same when either dicetylphosphoric acid or cardiolipin was used as the activator. This suggests that a certain critical negative charge density on the lecithin surface may be necessary for the commencement of the enzymic attack.

Evidence substantiating the theory that a negatively charged lecithin surface is necessary for enzyme action was obtained by studying its inhibition by metal ions such as UO_2^{2+}, Th^{4+}, and Ca^{2+}, which are efficient counter ion-binders of the negative groupings on a lipid surface[4]. Using a lecithin surface activated with dicetylphosphoric acid, it was shown that at the exact concentration of these ions necessary to neutralize the charge on the lecithin surface, the inhibition of enzymic activity became complete. In further experiments, positive amphipathic molecules were introduced into a negative surface of lecithin plus dicetylphosphoric acid particles by the gradual addition of cetyltrimethylammonium bromide, and here again there was a similar 'cut off' of enzymic activity just before the point at which the surface changed from being negatively charged to positive.

The question remained as to whether the negative charge on the surface of the substrate activated the actual attack of the enzyme on the lecithin surface or whether it merely solubilized the substrate by a detergent-like action, the subsequent enzymic attack occurring in the bulk phase. Microscopic examination of lecithin emulsions and high-speed centrifugation suggested that some dissociation of the lecithin particles into smaller micelles did occur with increasing concentrations of activator. However, there appeared to be no connexion between this more efficient emulsification and the development of the enzymic attack. Proof that the negative groupings were directly concerned with the actual enzymic attack on a lecithin surface was obtained by using surface films of yeast lecithin of high specific activity labelled with phosphorus-32. These films were introduced on the surface of a formate buffer at *p*H 3·3 and the counts per minute coming from the surface recorded with a mica end-window β-counter. The buffer was stirred magnetically from the underside so that any water-soluble glycerylphosphorylcholine produced by enzymic activity would be distributed throughout the bulk phase and its phosphorus-32-counts not recorded. With pure lecithin films injection of the enzyme into the bulk phase produced no change in the counting rate. When films were prepared from lecithin labelled with phosphorus-32 mixed with a small percentage of activator (for example, dicetylphosphoric acid, cardiolipin), there began a steady loss of radioactivity from the surface within a few minutes of the introduction of enzyme into the formate buffer. This loss was largely prevented by the addition of 0·02 *M* sodium fluoride to the bulk phase, a concentration which is sufficient to inhibit the enzyme almost completely. The loss of radioactivity was also not observed when the *p*H of the buffer was changed to 4·4, which is away from the optimum for enzyme activity. These experiments indicate that the enzyme acts directly on the activated surface of the lecithin film since any reaction occurring in the bulk phase would not be recorded by a change in the counting rate.

So far as we are aware, this is the first time that the activity of an enzyme has been directly related to the electrical (electrophoretic) charge on its substrate surface. The mechanism by which the lecithin surface becomes active when a critical density of negative polar groups is reached is not clear. Electrophoresis measurements on paper show that the enzyme is isoelectric at *p*H 3·3 so that the activation effect of the negative groups would appear to depend on orientation of the enzyme molecule within the diffuse ('double') layer rather than on simple electrostatic attraction and adsorption. This conclusion is supported by an observation that in the presence of the enzyme the lecithin surface remains negative, whereas, as is generally known, the non-specific adsorption of a protein at its isoelectric point on a negative surface leads to a masking of the charge.

In the inhibition experiments with metallic ions, it was observed that at concentrations of Th^{4+} or UO_2^{2+}, which were just insufficient to inhibit the enzymic activity, there was a distinct stimulation of the lecithinase action. This suggests the possibility that the metallic ions may initially mask negative groupings on the enzyme molecule itself, which would further assist the enzyme to orientate itself in relation to a negatively charged lecithin surface. If this is so, it would help to explain why the 'cut off' of enzymic activity with increasing amounts of these metal ions occurred when the lecithin surface was electrically neutral rather than at the critical negative charge density necessary for the development of enzymic attack. It is proposed to publish a fuller account of this work at a later date.

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LETTERS TO THE EDITORS

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Fall-out Radioactivity in a Deer's Antlers

The accumulation of radioactive material in biological structures as a result of fall-out from nuclear explosions presents a continuing and increasing problem in relation to human food supplies. It is now well established[1,2] that radiostrontium-levels in the bones of children are higher than in adults, and this is clearly related to the rate of deposition of 'new' calcium in the skeleton. The rapidity with which the antlers of deer are formed, coupled with the fact that these animals normally graze on upland pastures which are known to contain relatively high levels of fall-out radioactivity[1], suggested that antlers might well show particularly heavy contamination with radiostrontium. An opportunity was therefore taken during the course of a survey of radiostrontium-levels in foodstuffs to include for assay a pair of antlers from a deer shot on the island of Islay on November 3, 1957.

One complete antler was ashed, a strontium separation carried out with added carrier and the activity measured on a Geiger–Müller counter. The activity (strontium-89 plus strontium-90, and possibly active traces of other alkaline earths and heavy metals) was found to be 126 μμc./gm. of calcium present. At about the same time, a transverse section 2 mm. thick was cut from the other antler of the pair at one of the points of branching and applied in close contact with a piece of 'Kodirex' X-ray film. This was then exposed for 82 days in a light-tight box and the resulting autoradiogram is shown in Fig. 1.

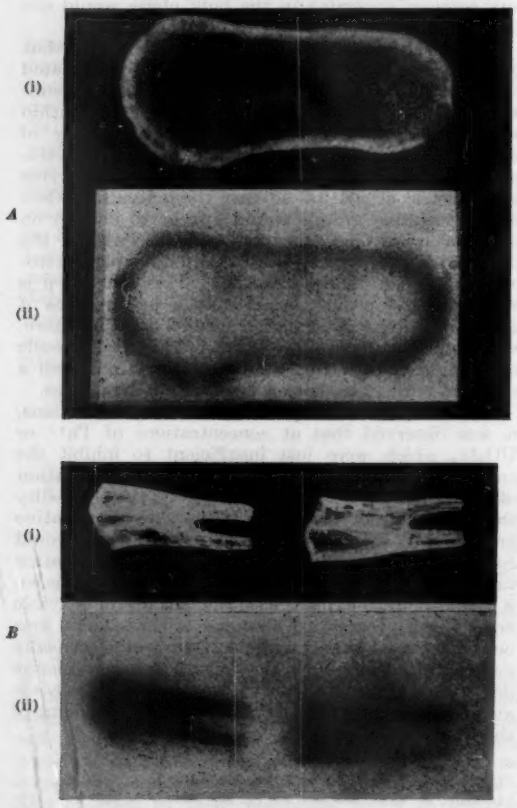

Fig. 1. *A*, Cross-section of deer's antler (i) and autoradiogram produced from it (ii). *B*, Two halves of a sheep's premolar from Ben Lawers, Perthshire (i) and the corresponding autoradiogram (ii)

A check on the distribution of activities between the two obvious concentric zones of the section was made by separating these two regions from a 2-in. length of the same antler and recovering the strontium from each. The results showed an activity in the dense peripheral zone of about nine times that in the central zone of spongy material, per unit area of cross-section.

We were later able to obtain a pair of antlers from a deer shot in the same area in 1952 for use in a control experiment. The strontium activity of this sample obtained by the same method as before was 11·2 μμc./gm. of calcium. Exposure of a similar section from these antlers to X-ray film for a period of 92 days produced a very slight image which was insufficient to allow photographic reproduction. It is therefore concluded that the major part of the blackening on the original autoradiogram is due to the longer-lived fall-out elements, in particular to the strontium isotopes.

We have since obtained autoradiograms of other biological structures, including a premolar of a sheep found dead at about 1,700 ft. on the side of Ben Lawers, Perthshire (see also Fig. 1) and of grass from the same area, which is known (unpublished work by Hawthorn, J., Stanwix, P. R., and Duckworth, R. B.) to contain high levels of radioactive strontium. We are not aware of the previous publication of autoradiograms of biological structures due purely to general fall-out radioactivity.

Our thanks are due to Dr. McGowan of Callumkill, Island of Islay, for supplying the antlers.

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Accumulation of Strontium-90 in Dental Tissues

Weanling rabbits given single injections of 500–1,000 μc. strontium-90 per kgm. showed a high frequency of tumours of the jaw[1], and preliminary histological studies suggest that they arose in close relation to the teeth. The amount of strontium-90 accumulated in individual teeth and in all teeth of one upper quadrant of the jaw after a single intravenous injection of 100 μc. strontium-90 per kgm. is given in Table 1. The amount of strontium-90 in the teeth is seen to increase with time after injection for at least thirty days and then to fall abruptly. The teeth of the rabbit grow continuously, and strontium-90 is lost because the layers in which the strontium is initially deposited erupt into occlusion and are later worn away in mastication. A similar

Table 1. STRONTIUM-90 IN TEETH AND FEMUR

No. of rabbit	Time interval between injection of strontium-90 and death	Individual teeth (mμc. per tooth) Incisors	Premolar 1st	Premolar 2nd	Molar 1st	Molar 2nd	Molar 3rd	Teeth (combined) from one jaw quadrant (μc.)	Femur (μc.)
993	8 hr.	82	42	40	120	90	81	0·45	4·6
996	24 hr.	63	61	71	99	100	52	0·45	4·1
999	3 days	110	51	71	130	73	68	0·50	3·0
997	9 days	120	86	120	120	120	99	0·67	2·2
998	30 days	110	74	130	150	130	100	0·70	1·8
1,000	90 days	33	12	33	43	32	27	0·18	—
970	180 days	3·0	1·9	2·4	2·3	3·2	1·8	0·015	0·91
992	180 days	7·7	2·2	4·3	5·1	4·7	3·6	0·028	0·87

sudden loss of strontium-90 from the teeth of the rat may be seen autoradiographically[2].

The initial increase with time after injection in the amount of strontium-90 in the teeth is in marked contrast to the steadily decreasing amount of strontium-90 in the femur (Table 1). This difference in behaviour between tooth and bone may be due to the substantial remodelling which occurs in bone but not at all in teeth, or because ion exchange in the mineral of bone is much greater than in the mineral of the teeth. In either case the liberation of strontium-90 from bone into the blood stream, during the days and weeks after a single intravenous administration, provides a continuously available source of strontium-90 for incorporation into the actively calcifying teeth, so that their strontium-90 content continues to increase with time until the moment when the first deposit reaches the masticatory surface and begins to be worn away. Thus the intensity with which the jaw is irradiated by a local radioactive deposit in the teeth may well be quite unrelated to general levels of deposition in bone.

This may be specially important in species like man, where the teeth do not wear away to the same extent as, and where strontium-90 incorporated into calcifying teeth will be much more permanently fixed than, in rodents.

One of us (W. H.) is indebted to the Royal Naval Physiological Laboratory, Alverstoke, for laboratory facilities and technical assistance. The help of Mr. R. H. Watts, of the Medical Research Council staff, is gratefully acknowledged.

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Shifts of Arc Lines at Various Pressures in Magnetic Fields

AN investigation of certain spectral lines emitted in a high-voltage arc between brass electrodes in nitrogen gas was made under pressures of from 1/7 to 85 atmospheres. The arc was run in and out of a magnetic field of 4,000 gauss. An empirical relation between the shift with and without a magnetic field at varied pressures for nine spectral lines has been found. There was a certain amount of scatter in the shifts of the lines, but among the hundreds of measurements of the spectral lines studied from Eastman Kodak spectrum analysis No. 2 plates, a significant pattern of shifts was found which differed for emission in a magnetic field from emission in a non-magnetic field.

Although the shift of any particular arc line under pressure is not steady the emergent pattern is quite evident. In all cases, the shift due to pressure in a magnetic field is less than in a non-magnetic field. With the exception of the first principal lines of copper, the shift of which seems to be anomalously changed by the magnetic field, lines most shifted by the pressure are most affected by the magnetic field.

In Fig. 1 pressure shifts of spectral emission lines of zinc, copper and lead in a magnetic and non-magnetic field are shown. It is apparent that, in addition to a decreased pressure shift in a magnetic field, the slopes of the lines for pressure shift versus pressure are less steep for emission in a magnetic than in a non-magnetic field. The ^3P–$^3P'$ lines of lead are an exception. Even for lead, the slope is not greater in a magnetic field. Lead lines were the only ones considered for which the coupling was j–j.

These results give considerable support to the theory that the normal van der Waals forces responsible for pressure shift are counteracted in a magnetic field by

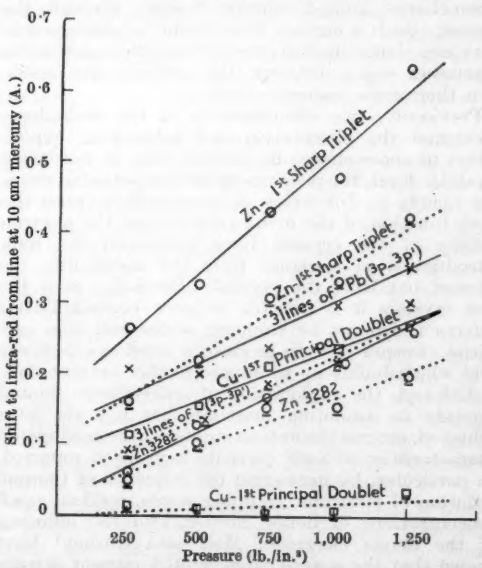

Fig. 1. Pressure shifts of arc lines: – – –, in the presence; ——— in the absence of a magnetic field. Curves are straight lines of best fit, through averaged points determined for zinc, ○; lead, ×; and copper, □. Underlined symbols refer to measurements in a magnetic field

space-charge forces. In a magnetic field, electrons and ionized metal gas ejected from the electrodes follow different paths between the high-voltage (5,000-V. a.c.) electrodes. It is suggested that a space charge made up of ions of vaporized metal is present in the space of the discharge when a magnetic field is applied. The magnetic field is perpendicular to the electric field between the electrodes. Motion of the charged particles is reversed by the a.c. electric field 120 times per second. In their much slower acceleration from zero velocity, the positive ions are diffused more than electrons by the force of the magnetic field transverse to their direction of motion.

The effect of the positive space charge is to increase the energy of electron transitions responsible for the spectral lines. The negative electronic charge belonging to an atom about to emit radiation is drawn farther from the nucleus by the surrounding positive-ion plasma. Pressure-shifted emission lines with a magnetic field will be to the violet side of pressure-shifted emission lines without a magnetic field.

This work was done at Fordham University, New York City, in 1955.

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Space-Charge Limited Currents in Insulating Materials

The modern theory of solids predicts that an electron can travel freely through the periodic potential field of a perfect crystal lattice provided that its energy lies within certain well-defined limits, or energy bands, which are characteristic of the crystal. A practical implication of this is that, if a sufficient number of such 'free' electrons can be introduced from a metal cathode into the allowed bands of an insulating crystal, it should be possible to obtain a space-charge limited current flowing through the crystal. Such a current flow would be analogous to the space-charge limited current which flows across the evacuated region between the cathode and anode in a thermionic vacuum diode.

Previously, two circumstances in the main have prevented the observation and subsequent exploitation of space-charge limited currents in insulating crystals. First, the presence of surface potential steps, due mainly to differences in magnitude between the work function of the metal cathode and the electron affinity of the crystal, have prevented the bulk introduction of electrons from the metal into the allowed bands of the crystal. Secondly, even the best crystals it is possible to grow contain lattice defects which act as trapping states and trap any initial electron flow to produce a fixed space-charge field which builds up to oppose further current flow.

Although the exploitation of space-charge limited currents in insulating materials has not yet been achieved, several theoretical studies of the anticipated characteristics of such currents have been reported. In particular, by neglecting the influence of thermal diffusion of electrons, trapping states, residual small concentrations of donor centres, and the influence of the anode electrode, Mott and Gurney[1] have shown that the space-charge limited current density should be given by $J = 9\varepsilon\nu V^2/8d^3$ amp./m.^{2}, where ε is the absolute permittivity and d is the thickness of the insulator, and ν is the mobility of the electrons in the insulator. At sufficiently high applied voltages the whole of the space-charge in the insulator should be drawn across. The current should then become proportional to voltage, since the drift velocity of the electrons would be proportional to the applied field. Under these conditions the current density should be given by $J = e\nu N_0 V/d$ amp./m.^{2}, where N_0 is the space-charge electron density in the insulator at the surface in contact with the cathode, and the approximate transition voltage between space-charge limited and proportional currents should be given by $V_e = 8ed^2N_0/9\varepsilon$ volts. These calculations have been extended by Lampert[2] to include the effects of deep trapping states. His equations show that as the applied voltage is increased the current flow should initially be very small, but should rise extremely rapidly at a certain critical voltage to reach the space-charge limited value at an applied voltage given approximately by $V_t = ed^2N_t/2\varepsilon$ volts, where N_t is the density of trapping states. A further case of interest has been studied by Skinner[3], who has considered the flow of current in an ideal insulator bounded by two metal electrodes of different work functions. These calculations indicate, as expected, that current rectification should be obtained.

These anticipated properties of space-charge limited currents in insulating materials suggest the exploitation of these currents to develop a new class of solid state devices[4]. Experiments to this end have been made in my laboratories during the past two years and the expected characteristics of these currents have been demonstrated in crystals of cadmium sulphide.

Fig. 1 shows the steady current – voltage characteristic of a thin crystal plate about 3×10^{-3} cm. thick. The crystal was provided with a cathode of indium metal about 1 mm.^{2} in area, vacuum-welded to one surface, and an anode, in the form of a coating of colloidal graphite, on the other surface. The curve

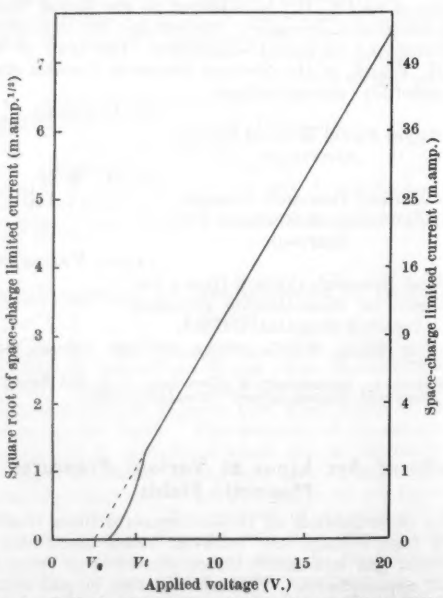

Fig. 1. Current – voltage characteristic of space-charge limited current in a cadmium sulphide crystal. The curve shows the relation between the square root of the current and the applied voltage

shows the forward current characteristic for this crystal measured at room temperature (20° C.) and is typical of the results obtained so far. Photoconductive effects were eliminated by enclosing the crystal in a light-tight container. As the applied voltage was raised no current-flow could be detected ($i<0{\cdot}05$ μamp.) until a voltage $V_0=2{\cdot}5$ volts was reached. The presence of this threshold voltage is attributed basically to the difference in magnitude between the electron affinity of the crystal and the work function of the anode; this difference must be overcome by the applied voltage before appreciable current can flow. As the applied voltage was increased further a very small current commenced which then rose rapidly to about 2 m.amp. at a voltage $V_t=5{\cdot}7$ volts. In this region considerable time was required for the current flow to reach a steady value and the current – voltage curve was quite steep up to the space-charge limited value. These characteristics are attributed to the influence of deep trapping states. This measured value of V_t indicates that the density of deep trapping states in this crystal was of the order of 10^{13} per cm.^{3}, which is satisfyingly low. For higher voltages the current flow was quite steady and reproducible provided that thermal effects due to power dissipation were avoided. In this region the precise square-law characteristic expected for space-charge limited currents was obtained. From the slope of this part of the curve the mobility of the electrons in the crystal was found to be approximately 500 cm.^{2}/V. sec. This is a rather high figure for cadmium sulphide, but is probably explained by the relative freedom of this particular crystal from lattice defects and trapping states.

In order to supply the magnitudes of space-charge limited currents observed, the electron space-charge density N_0 in the crystal at the surface in contact with the cathode must have been of the order of 10^{18}/cm.^{3}. This implies that the conduction band of the crystal at the cathode was within 0·05 eV. of the Fermi-level of the cathode metal.

In the reverse direction the crystal was, as expected, an insulator. At applied voltages up to 20 V. the current flow was undetectable with a sensitive galvanometer, indicating a reverse resistance greater than 10^{11} ohms. At 80 V. the reverse resistance was still of the order of 10^{10} ohms.

These various properties of current flow in insulators make this a worthwhile field for fundamental studies and for the design and development of new solid state devices. For example, much information can be obtained about lattice defects in dielectric crystals by studying electron trapping and scattering; the electron affinities of dielectric crystals can be measured directly, giving useful information to assist theoretical studies of crystal and surface structures; and the nature of contacts between conductors and insulators can be examined directly. From the point of view of the developing devices the exploitation of space-charge limited currents in insulating materials is attractive for many reasons apart from the promise of many new types of devices. For example, by working under space-charge limited conditions, relative insensitivity to changes in temperature should be achieved; this is an appreciable advantage for a solid state device.

As yet only preliminary experiments and measurements have been made and it is certain that many problems have to be solved before successful and reliable devices can be designed. Even so it seems clear that the study of space-charge limited current flow in insulating materials will be a fruitful field for fundamental investigations and will lead to the development of many new types of solid state devices.

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Effects of Electron Bombardment upon Sodium Tetraborate and Boric Acid in an Electron Microscope

The specimens under observation in the electron microscope are exposed simultaneously to a high vacuum and to electron bombardment. Under these conditions, the specimens may lose volatile constituents due to the combined effects of the vacuum and of the temperature rise[1,2]; also the crystal structure may undergo alterations as a result of exposure to the electron beam[3].

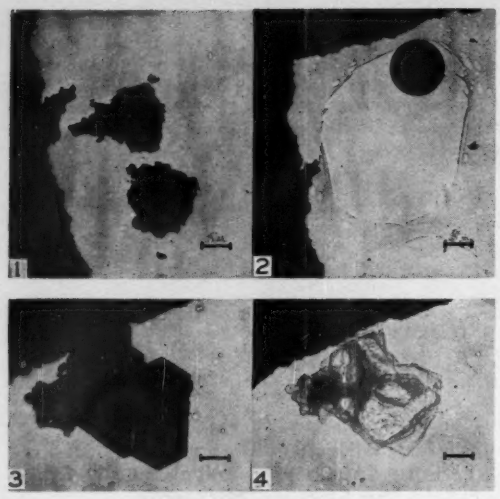
A systematic study was conducted on the effect of electron bombardment upon crystals in an electron microscope, especially on acetates, carbonates, oxalates and some crystalline organic acids (Souza Santos, H. L., unpublished work). This study was intended to correlate the morphological changes in the crystal which are observable with the electron microscope and the physical and chemical transformations with the temperature rise which can be expected from the chemical composition of these substances.

In the course of these studies, some observations on the behaviour of sodium tetraborate and boric acid were made which are of interest in view of the similarity of the effects of temperature of these substances[4].

Sodium tetraborate dissolves in its own water of crystallization at 75° C. at atmospheric pressure; it loses five molecules of water at 100° C. and nine at 150° C., becoming anhydrous and melting at 320° C. On further heating, it swells up to a spongy mass; at a higher temperature, this mass runs together, forming a clear colourless glass—borax glass—the melting point of which is reported[5] to be between 561° and 878° C.

Boric acid, when heated to 70° C., loses no water; at 100° C., it loses two-thirds of its water and at 160° C. it melts, forming dihydrotetraboric acid ($H_2B_4O_7$). At a higher temperature, the acid froths up, losing its water and forming a fused viscid mass of anhydride, which on cooling congeals to a transparent but fissured glass. At a red heat, boric acid loses all its water with much bubbling[4].

From their physico-chemical properties, it could be predicted that sodium tetraborate and boric acid would give similar effects under electron bombardment, namely, melting of the crystals, formation of spherical drops or reunion of many drops into a single one, loss of water as vapour accompanied by bubbling, residues of borate glass and boric anhydride.



Figs. 1 and 2. Sodium tetraborate crystals before and after bombardment

Figs. 3 and 4. Boric acid crystals before and after bombardment
Scale : 5μ

The following method was used for preparing the specimen. Dry powdered samples of analytical grade boric acid (H_3BO_3) and sodium tetraborate ($Na_2B_4O_7.10H_2O$), were deposited on nickel grids covered with 'Parlodion'; the excess solid was removed by turning the grids upside down, thus leaving some minute crystals adhering to the plastic. An *RCA* type *EMU* electron microscope operating at 50 kV. with self-biased gun was used. The lowest possible current intensity was used at first, and this was raised until the morphological changes appeared. Wherever possible, electron micrographs were taken at the initial, intermediate and final stages of bombardment.

Under electron bombardment the particles of sodium tetraborate seem to melt, giving spherical drops; when many particles are in contact the drops aglomerate into a single drop, as do liquid drops, due to surface tension. Fig. 1 shows sodium tetraborate particles taken with a low-intensity electron beam. Fig. 2 shows the same particles after strong bombardment; the particles are united into one almost spherical particle.

In the electron microscope electronically dense particles of boric acid lose their opacity to electrons, leaving transparent envelopes, which retain the original shape of the particles. Fig. 3 shows some boric acid crystals in an early stage of bombardment; a region is becoming transparent; before bombardment the whole crystal was quite opaque. In Fig. 4 the same crystal shows only the residual transparent envelope after strong bombardment.

The predictions were confirmed in the case of sodium tetraborate, but not for boric acid, the behaviour of which is that of a completely volatile material; this contradiction could be explained by the fact that boric acid is relatively volatile in steam[1,6]; its vapour pressure is 242 mm. of mercury at 128° C., this temperature being in the range of calculated values for specimens in an electron microscope[7].

Further studies are in course and will be published elsewhere.

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Origin of Tektites

In the recent controversy concerning the origin of tektites[1,2], Kopal has given reasons for considering that they must be formed close to the terrestrial surface, and regards these as grounds for favouring Urey's cometary theory[3]. It appears useful to direct attention to another suggestion which may have been overlooked—the 'plastic sweeping' theory of Hardcastle[4].

Briefly, Hardcastle suggests that tektites have been formed from stony meteorites by the process of ablation during their passage through the atmosphere. The glazed surface of these meteorites is considered to contain an enriched content of silica, and to be swept away piecemeal during flight. The solidified remnants land as tektites. The considerable ablation known to take place, and the comparatively long-lived trails observed in stony meteorite falls are adduced to support the theory. Attention is also directed to the marked pitting of the stones and the size of the pits.

An analysis of the glazed surface material would enable a test of this suggestion to be made. It might be expected to contain a selective sample of the material of the meteorite rather than to reflect the average composition. In view of Urey's statement that "the chemistry of silicate material is not completely known", such an analysis would provide additional relevant data.

The 'plastic sweeping' theory appears to explain: (1) the derivation of tektite material from meteorites of known composition; (2) a rapid heating process capable of producing the observed physical forms; (3) an explanation of the wide scattering. The most serious objection appears to be the limited time-scale within which tektite falls are known to have taken place. Urey, on the other hand, appears to consider two comets only, one in Eocene time, which produced the bediasites, and the other in the Pleistocene, producing the other falls. Even granting the possibility of fragmentation of the cometary nucleus, it seems doubtful whether the observed distribution is satisfactorily explained. In these respects, the lunar impactite theory is superior.

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Determination of Hammett Sigma Constants by Intramolecular Hydrogen Bonding

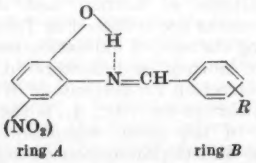
THE extensive literature that exists concerning Hammett's σ-constants has been subjected to several recent reviews, including a compilation and examination of available data[1], a discussion of the significance and limitations of the concepts involved[2], and an attempt to deduce best values and probable errors for the σ-values[3]. In most cases σ-values have been determined by examination of equilibrium constants or reaction-rate constants of substituted benzene derivatives, thus requiring consideration of product states or transition states. In the few instances where examination of the native (unreacted) molecule has led to a determination of σ (via physical measurements), the site examined has invariably been attached directly to the ring carrying the groups under study, thereby still exerting some influence (other than electronic) on the effect measured as well as excluding the *ortho*-position for steric reasons.

Table 1

Substituent (ring *B*)	σ-*ortho*	σ-*meta*	σ-*para*
F	+ 0·17 (*a*)	+ 0·31 (*a*) + 0·337	+ 0·15 (*a*) + 0·062
Cl	+ 0·22 (*a*)	+ 0·38 (*a*) + 0·373	+ 0·20 (*a*) + 0·17 (*b*) + 0·227
Br			+ 0·25 (*a*) + 0·24 (*b*) + 0·232
CH_3	− 0·14 (*a*)	− 0·07 (*a*) − 0·069	− 0·14 (*a*) − 0·170
NO_2		+ 0·75 (*a*) + 0·710	+ 0·778
OH	*	+ 0·05 (*a*) + 0·121	− 0·32 (*a*) − 0·37
OCH_3	− 0·34 (*a*)	+ 0·04 (*a*) + 0·11	− 0·28 (*a*) − 0·27 (*b*) − 0·268
$N(CH_3)_2$			− 0·80 (*a*) − 0·91 (*b*) − 0·83

Values (*a*) obtained with ring *A* unsubstituted, with carbon tetrachloride as solvent ($K = 0·033$). Values (*b*) obtained with a 4-NO_2-group in ring *A*, with methylchloride as solvent ($K = 0·033$). Unmarked values are from ref. 3 for comparison.
* Unobtainable due to the preferred hydrogen bonding from the ring *B* phenolic hydroxy group.

A method has been devised which permits estimation of the Hammett σ-constant in a manner circumventing many of these objections. In the system:



ring *A* ring *B*

the group being investigated (*R*) is physically isolated from the O—H · · · N hydrogen bond regardless of its position on ring *B*. Its effect on the basicity of the nitrogen may be measured, none the less, by the strength of the hydrogen bond on the phenol group of ring *A* as determined by the exact frequency of the O—H stretching vibration. Table 1 shows various σ-constants obtained from the expression:

$$\sigma = \Delta\nu_{OH} \cdot K$$

where $\Delta\nu_{OH}$ is the frequency shift of the substituted homologue (in wave-numbers) compared with the unsubstituted parent compound, and K is a factor employed to bring these wave-number shifts into the range of the classic Hammett σ-values.

The figures above show that when steric effects are eliminated, the *ortho* and *para* σ-constants are nearly the same. A more elaborate discussion of the principles involved, and a description of experimental detail, will be published elsewhere.

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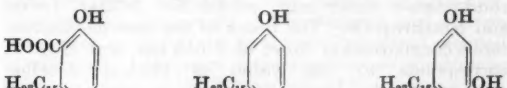
Surface-active Characteristics of Sodium Anacardate isolated from Cashew Nut Shell Oil

CASHEW nut (*Anacardium occidentale* Linn.) shell liquid obtained from unroasted shells was found by Stadeler[1] to consist chiefly of anacardic acid (*A*) (on heating, this is decarboxylated to cardanol (*B*)), a salicylic acid derivative with a long unsaturated side-chain in the position *ortho* to the carboxyl group, and cardol (*C*), a resorcinol derivative with a similar side-chain. Smith[2] showed that the unbranched side-chain consisted of 15 carbon atoms and 2 double bonds; other workers[3] have shown that the oily liquid is really a mixture of saturated and mono-, di-, and tri-olefinic compounds in proportions that give, on average, about two double bonds per molecule. Although the surface-active properties of the sulphonated shell liquid have already been studied[4], no thorough investigation has yet been carried out on anacardic acid, which, being an arylalkyl surfactant and a promising bactericidal agent, needs special attention[5]. Results of a preliminary study on sodium anacardate as a surfactant and bactericidal agent are reported here.



(*A*) (*B*) (*C*)

Shell liquid extracted with 95 per cent ethyl alcohol was saponified and the non-saponifiable material was removed by extraction with ethyl ether. Stage-wise liberation of cardol and then of anacardic acid (followed by separate extractions with ethyl ether), was carried out by passing carbon dioxide and treating the solution with dilute hydrochloric acid respectively. Dark brown anacardic acid, obtained after evaporation of the ether, and purified by charcoal treatment, had the following characteristics: specific gravity (30° C.), 1·0001; refractive index (40° C.), 1·5205; iodine value (Wij, 30 min.) 177·0 (this includes halogen substitution in the aromatic ring); iodine value determined by the corrected method of Kale and Kamath[6], 124·4. On the basis of the average molecular weight of anacardic

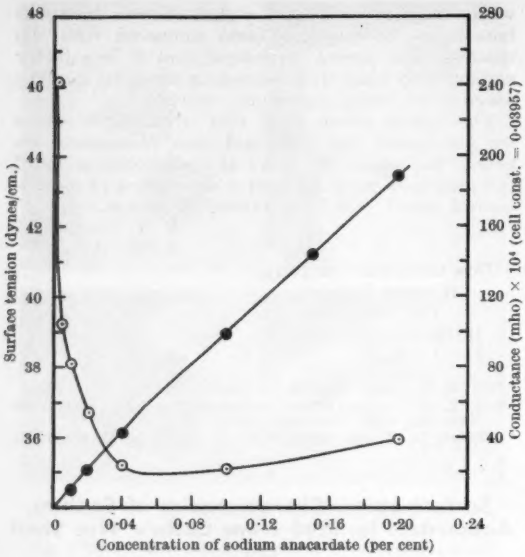


Fig. 1. ○, Surface tension; ●, conductance

acid being 344, this gives an average of 1·686 double bonds per molecule.

On hydrogenation in the presence of a platinum catalyst a 95 per cent yield of white tetrahydroanacardic acid (m.p. 91·0° C.) was obtained. An alcoholic solution of anacardic acid was neutralized with slightly less than the requisite amount of alcoholic sodium hydroxide. After evaporation of most of the alcohol, the thick solution was poured into dry acetone, when the disodium salt precipitated out; this was filtered off, washed with dry acetone and dried *in vacuo*. The various surface-active properties of sodium anacardate were as follows:

(*a*) Surface tension at 25° C. (determined by Du Nuoy's tensiometer) of a 0·1 per cent solution was 35·1 dynes/cm. The surface tension/concentration curve showed a minimum in the concentration range 0·02–0·1 per cent (Fig. 1).

(*b*) The conductances of solutions of varying concentration were determined at 25° C. using a conductance meter unit, model No. 263941, Leeds and Northrup Co. The break of the specific conductance concentration curve at 0·053 per cent (Fig. 1) corresponds to the value of critical micellar concentration.

(*c*) While the interfacial tension of water against *n*-heptane was 51·24 dynes/cm. at 25° C. (Du Nuoy's tensiometer), 0·01, 0·02, 0·05 and 0·10 per cent sodium anacardate in aqueous solution lowered the value to 30·47, 20·07, 8·88 and 4·49 dynes/cm. respectively.

(*d*) 15 ml. of a 0·1 per cent solution when shaken with a 5 ml. *n*-heptane in a 25 ml. stoppered measuring cylinder (height 13 cm. and internal diameter 1·75 cm.) for 1 hr. in a shaker which had an amplitude of vibration of 11 cm. and imparted on the average 110 to-and-fro motions per minute. This emulsified the hydrocarbon almost completely. The volumes of aqueous and emulsion layers after intervals of 5 min. and 3 hr. were 13·8 ml., 5·8 ml. and 14·50 ml. and 5·10 ml. respectively. Average surface areas per unit volume of oil droplets, in 150 min.- and 24 hr.-old emulsion samples, calculated from the size distribution of the oil droplets[7], were $2·839 \times 10^3$ cm.²/c.c. and $2·005 \times 10^3$ cm.²/c.c. respectively. The figures denote excellent emulsion stability.

(*e*) When 200 ml. of a 0·1 per cent solution were discharged from a pipette (internal diameter of nozzle 1 mm.) on to a cushion of 50 ml. solution of the same concentration placed at the bottom of a long cylinder (internal diameter 45 mm.), the average height of fall being 75 cm., the foam heights at 0 min. and 30 min. were 16·8 cm. and 15·1 cm. respectively.

(*f*) Phenol coefficients of sodium anacardate with reference to *B. typhosa* and *S. aureus* were found to be 1·07 and 4·00 respectively. The concentrations of sodium anacardate solutions needed to kill the micro-organisms were of the same order, the large difference in the two values being due to the relatively weak influence of phenol on *S. aureus*.

These observations, coupled with the fact that sodium anacardate does not irritate the skin, indicate its suitability as a bactericidal surfactant. The inferior surface-active properties of sodium tetrahydroanacardate suggest that the ethylenic bonds were largely responsible for the greater solubility in water and the superior surface-active properties of sodium anacardate. The details of the investigations will be reported elsewhere.

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Kinetic Isotope Effect in the Iodination of Aromatic Amines

We have determined the kinetic isotope effect in the iodination of many aromatic amines, aminocarbonic and aminosulphonic acids by comparing the iodination-rates of normal and deutero-compounds. The results are collected in Table 1, the isotope effect being the ratio of iodination-rate constants, k_H and k_D, of normal and deuterated compounds without any correction for percentage of substitution of H by D). Relative activity, A_r, is the ratio of the rate constant of the given compound to that of iodination of *m*-dimethylaminobenzenesulphonate ion taken as 1.

Table 1 shows that *m*- and *p*-dimethylaminobenzenesulphonates are iodinated without any isotope effect ($k_H/k_D = 1$). 2,4,6-trideutero-*m*-aminobenzoate ion is iodinated slightly more slowly than the light compound. The iodination of other amino compounds is connected with a considerable isotope effect.

Similar isotope effects are observed in other cases of electrophilic substitution in aromatic compounds[1–3].

Table 1

Substance M	Substitution of H by D (per cent)	k_H/k_D	Relative activity, A_r	Experimental conditions: initial molar concentrations, pH, temperature (deg. C.)
2,4,6-Trideutero-*m*-dimethylaminobenzenesulphonate ion	90	1	1	M 0·076; I_2 0·008; KI 0·04; 25°
4-Deutero-1-dimethylaminobenzene-3-sulphonate ion	61	1	1	M 0·0145; I_2 0·0072; KI 0·073; phosphate 0·064; *p*H 7·0; 25°
2,6-Dideutero-1-dimethylaminobenzene-4-sulphonate ion	90	1	0·2	M 0·027; I_2 0·005; KI 0·01; 25°
2,4,6-Trideutero-*m*-dimethylaminobenzoate ion	95	1·4	35	M 0·02; I_2 0·005; KI 0·4; 30°
2,4,6-Trideutero-metanilate ion	61	2*	0·02	M 0·133; I_2 0·015; KI 0·036; 35°
2,4,6-Trideutero-*m*-aminobenzoate ion	90	4·8	0·22	M 0·045; I_2 0·005; KI 0·05; 30°
,,	90	3	0·24	M 0·025; I_2 0·005; KI 0·05; phosphate 0·05; *p*H 7·2; 30°
2,4,6-Trideutero-aniline	86	3·5	5·4	M 0·05; I_2 0·005; KI 0·15; 25°
,,	86	4·0	15	M 0·02; I_2 0·004; KI 0·12; phosphate 0·025; NaCl 0·08; *p*H 7·6; 25°
2,4,6-Trideutero-methylaniline	95	3·2	110	M 0·01; I_2 0·002; KI 0·3; acetate 0·05; *p*H 5; 25°
2,4,6-Trideutero-dimethylaniline	89	3·0	120	M 0·01; I_2 0·002; KI 0·15; lactate 0·5; *p*H 3·5; 30°

* This value of k_H/k_D is probably much smaller than the real one, because the percentage of substitution in the preparation used was not high

In a discussion of these results it is necessary to take into consideration the form of the general kinetic equation of iodination of aromatic amines[4], namely:

$$-\frac{d(I)}{dt} = k[M]^2[X] + k'[M][X][B] \qquad (1)$$

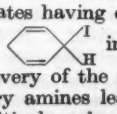
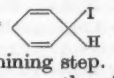
where M is an aromatic amine, X iodine cation or molecular iodine and B a basic component of the added buffer salt.

Equation (1) suggests that the activated complex of the reaction contains a base in the form of B or the second molecule M. One may suppose that the base acts as a proton acceptor in substitution in the benzene nucleus. However, the absence of isotope effect in iodination of dimethylaminobenzenesulphonate ions rules out this mechanism, at least in this case, because this assumption requires the proton elimination reaction as rate-determining step.

The alternative is that iodinating agents act in the form of complexes with bases $X \cdots M$ or $X \cdots B$, but that the hydrogen-splitting step does not limit the reaction-rate.

One could explain the isotope effect in iodination of other amines by supposing that bases act in these cases as proton acceptors; but considering the very great similarity of kinetic relations in iodination of various amines, we think that in all cases of iodination the base reacts in the form of a complex with I^+ or I_2. This assumption is supported by the consideration that the concentrations of (hydrated) iodine cation in the presence of potassium iodide are extremely small. Using Bell and Gelles data[5], it is easy to calculate that the iodine cation concentration in our experiments was as low as 10^{-14}–10^{-15} M. These concentrations cannot account for the observed rates of iodination of the most active amines.

At present, we cannot explain positively the established differences in k_H/k_D values in the iodination of aromatic amines. Table 1 shows that there is no connexion between the isotope effect and the iodination-rate. Indeed, the cases of presence or absence of isotope effect belong equally to high and to low values of A_r.

Grovenstein and Kilby[2] think that isotope effect in aromatic substitution is connected with the formation of stable intermediates having quinonoid structure, for example, O =  in the iodination of phenol, but the discovery of the isotope effect in the iodination of tertiary amines leads to the conclusion that the positively charged complexes $R_3\overset{+}{N}$ =  can also lose a proton as the rate-determining step.

However, the structural possibility of the formation of such intermediates is insufficient for the appearance of an isotope effect because, as we have seen, the introduction of a sulphonic group into the molecule of a tertiary aromatic amine results in disappearance of this effect. Apparently one must take into account the energetic pecularities of a reacting aromatic molecule.

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Crystalline Sodium Hyaluronate

Most hyaluronates in living tissues are in the form of protein complexes. Physical-chemical investigations on these complexes yield results which differ, depending on the source of the material and also on the extent to which the hyaluronic acid was purified of proteins[1]. It appears necessary that, in addition to the descriptions of the divergences of these complexes, one should investigate the nature of the complexing itself. Two views are prevalent in this matter. Noguchi[2] advocates a pure electrostatic interaction between protein and polyuronide, and Partridge[3] believes that the polyuronides have an orienting effect on proteins upon complexing. The last view presupposes certain stereospecific interactions besides electrostatic forces. Although hyaluronates are known to be birefringent and electron-microscopic investigations indicate a fibril structure[4], X-ray diffraction studies have so far proved that hyaluronic acid films or fibres are of amorphous nature.

Sodium hyaluronate was isolated from umbilical cords by a combination of processes (pepsin and trypsin digestion, Sevag process, extraction of sulphated polyuronides with ammonium sulphate and pyridine, final removal of protein by Lloyd's reagent). The resulting material was homogeneous

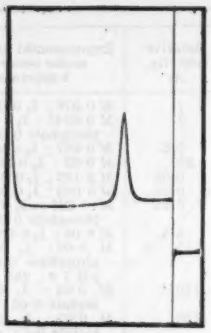

Fig. 1. Sedimentation pattern of sodium hyaluronate in 1 per cent aqueous sodium chloride solution

as observed in ultracentrifuge (Fig. 1), and had a weight average molecular weight of 70,000. This low molecular weight, as compared to 1–4 million obtained by other authors[5] indicates that the complete removal of proteins from the preparation is achieved only at the expense of the hyaluronate chain. Although glucuronic acid and sodium were present in the preparation close to the theoretical amounts, both micro-Kjeldahl nitrogen and photocolorimetric analysis of N-acetyl glucosamine indicated that beside depolymerization a loss of nitrogen might have occurred to the extent of at least 10 per cent. However, the preparation was free from proteins and from sulphate-containing polyuronides.

Sodium hyaluronate dried from ethanol precipitation and humidified to 10 per cent moisture content yielded a highly crystalline powder diagram with as many as 22 observable reflexions (Fig. 2). The two different exposure times on the photograph were employed to show the higher order of reflexions. Detailed crystallographic analysis of the structure of sodium hyaluronate will be published shortly.

The fact that sodium hyaluronate containing approximately 3 per cent of protein (sample from the last purification step) yields an amorphous X-ray diagram indicates that the protein is strongly bound to the polyuronides, being attached at frequent spacings, and therefore, it disrupts the three-dimensional lattice array even if it is present in small quantities.

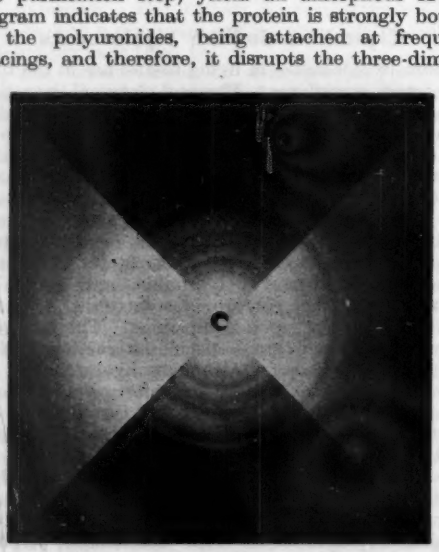

Fig. 2. X-ray powder diagram of sodium hyaluronate. Copper $K\alpha$ radiation. Camera distance, 5 cm. Reduction, 1/2

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Changes in Ultra-Violet Absorption Spectra of Deoxyribonucleic Acid by Treatment with Bromine

In 1947, a procedure was developed[1] for the determination of pyrimidine nucleoside in which bromination and prolonged acid hydrolysis precede the performance of Bial reaction. More recently, it was also shown that marked changes in ultra-violet absorption spectra, particularly disappearance of selective absorption of cytosine, uracil and their nucleosides, occurred before and after the bromination of the compounds[2]. While studying the effects of bromine on the chemical nature of nucleic acids, we have also found that the maximal absorption of deoxyribonucleic acid shows a decrease with increasing bromination period. In further experiments, it has also been demonstrated that acid hydrolysis of brominated deoxyribonucleic acid results in a loss of selective absorption without significant loss of phosphorus.

White fibrous sodium deoxyribonucleate of herring sperm giving a negative biuret test was prepared[3] by deproteinization[4] from a commercial one (Minophagen Pharm. Co., Ltd., Tokyo). The preparation showing the analytical data of 8·6 per cent for phosphorus[5] and 14·9 per cent for nitrogen (Kjeldahl–Parnas) was used throughout this study. 60 ml. of 0·3 per cent sodium deoxyribonucleate solution and an equal volume of 2 per cent bromine water preincubated separately at 37° C. for 10 min. were combined in a tightly glass-stoppered flask. Immediately after mixing, the reaction mixture was incubated at 37° C. with occasional shaking. 10-ml. aliquots withdrawn at intervals were vigorously aerated for 3 min., when the solution became almost colourless. A few drops of diluted aqueous ammonia were then added to eliminate free bromine completely and to adjust *p*H at around 6. Mixtures thus treated were transferred to each 'Cellophane' bag for dialysis against running tap water (below 12° C.) for 2 days then against frequent changes of distilled water in the cold until no ammonium salt could be detected (Nesseler test) in the dialysate (about 3 days were needed). Inside liquid and washings were combined and distilled water was added to a final volume of 20 ml. 10-ml. portions of each solution were adjusted at *p*H 1·5 (glass-electrode) by dropwise addition of 2 *N* hydrochloric acid, when little or no turbidity occurred with brominated deoxyribonucleic acid whereas prompt precipitates arose with non-treated ones. After 30 hr. incubation at 37° C., solutions were placed in each 'Cello-

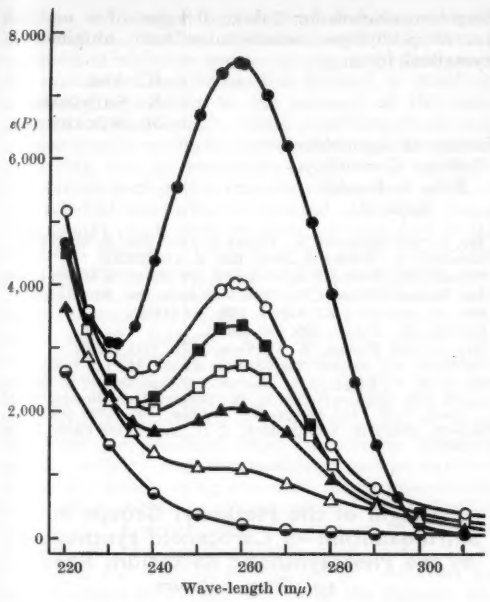

Fig. 1. Ultra-violet absorption spectra of brominated deoxyribonucleic acid in 1/15 *M* phosphate buffer of *p*H 7·0. Bromination period: 0 (original acid), —●—; 1·5 min., —○—; 3 min., —■—; 1 hr., —□—; 2 hr., —▲—; 5 hr., —△—; 12 hr., —◒—

phane' bag to dialyse as mentioned above and the final volume was made up to 20 ml. by the addition of distilled water. Solutions thus treated were then measured for ultra-violet absorption spectra with a Beckman-type spectrophotometer, phosphorus according to Fiske and Subbarow[6] and nitrogen by the method of Kjeldahl–Nesseler[7].

From Fig. 1, showing typical changes in absorption spectra resulting from the bromination of deoxyribonucleic acid, no major shift will be seen in the absorption maxima so long as the acid was treated for a short time; however, $\varepsilon(P)$ decreased with the increase of time to a complete loss of the selective absorption. Furthermore, as depicted in Fig. 2, the remaining absorption of brominated deoxyribonucleic acid was completely removed by the treatment with hydrochloric acid. Since the brominated acid was hydrolysed under the same conditions as employed for the preparation of apurinic acid and compounds, the spectra of which are given in Fig. 2, and had a nitrogen content similar to that of apurinic acid (N : P = 0·55)[3], it may be concluded that the pyrimidine moiety in brominated deoxyribonucleic acid was not liberated upon hydrolysis under the conditions employed and hence, extinction of brominated deoxyribonucleic acid was contributed by the purine moiety. On the other hand, diminution of nitrogen content was accompanied by the abatement of extinction with increasing bromination period. However, short bromination lessened markedly the absorption without significant loss of nitrogen. Decrease in quantity of nitrogen may be caused by the acidity of bromine water as a result of the liberation of purine bases. In all cases, the recovery of phosphorus was almost quantitative (more than 90 per cent) and the colour yield of the reaction of brominated deoxyribonucleic acid with diphenylamine[8] did not decrease within 20-min. bromination when comparison was made on the basis of phosphorus content.

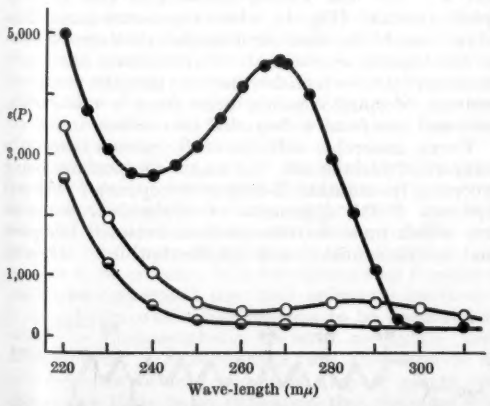

Fig. 2. Ultra-violet absorption spectra of brominated deoxyribonucleic acid hydrolysed with hydrochloric acid (in 1/15 *M* phosphate buffer of *p*H 7·0). Bromination period; 0 (apurinic acid), —●—; 1·5 min., —○—; 12 hr., —◒—

Although the mode of action of bromine on deoxyribonucleic acid still remains uncertain, these results clearly indicate that bromine exerts a distinct influence particularly on the ultra-violet absorption spectra, and deoxyribonucleic acid gives a derivative devoid of any absorption characteristics of nucleic acids by a short bromination followed by mild acid hydrolysis.

Yeast ribonucleic acid showed rather different behaviour from deoxyribonucleic acid towards bromine treatment. Further work is now in progress and details will be published elsewhere.

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Preparation of Kojibiose

Previously, we detected kojibiose (2-O-α-D-glucopyranosyl-D-glucopyranose) in *sake* and its *moromi* and isolated it from a mixture of oligosaccharides synthesized from maltose and glucose by the culture filtrates of *Aspergillus oryzae*[1], *Asp. niger*[2] and *Schizosaccharomyces pombe*[3]. It was also isolated from hydrol[4]. Sato and Aso[5] crystallized it as α- and β-octaacetates, and Matsuda[6] and Haq and Whelan[7] synthesized it chemically.

The proportion of kojibiose in the sources was very small. Moreover, the separation of kojibiose from

other disaccharides, especially *iso*maltose, by preliminary carbon column chromatography, was very difficult, as was its synthesis.

This communication deals with the preparation of kojibiose. Previously, it was reported[8] that when the dextran-producing organism *Leuconostoc mesenteroides* is grown on a medium containing sucrose, in the presence of large amounts of 1,4-α-linked glucose polymers, 1,6-α-linked oligosaccharides are produced in appreciable quantities. A particularly interesting example was that of Bailey *et al.*[9], who isolated, by charcoal chromatography, a new trisaccharide from a culture of *Betacoccus arabinosaceous* (Birmingham strain), which had been grown on a medium containing yeast extract, inorganic salts, sucrose and lactose. They determined its structure as O-β-D-galactopyranosyl-(1→4)-O-[α-D-glucopyranosyl-(1→2)]-D-glucopyranose. They reported that cleavage of the β-linkage in the trisaccharide by almond β-glycosidase was extremely slow, and that some 50 per cent of the trisaccharide remained after three weeks. They did not isolate kojibiose in a crystalline form.

Fig. 1. *a*, α-Kojibiose octaacetate; *b*, β-kojibiose octaacetate

Considering the structure, if the 1,4-β-linkage (lactose) in the trisaccharide is cleaved by *Saccharomyces fragilis* lactase, kojibiose and galactose will be easily obtained. By this method we obtained kojibiose in almost theoretical yield.

A culture of *Leuconostoc mesenteroides* (dextran-producer) instead of *Betacoccus arabinosaceous* (Birmingham strain) was prepared in a medium containing the following ingredients per l.; sucrose 30 gm., lactose 100 gm., ammonium sulphate 0·6 gm., potassium phosphate 5 gm., sodium chloride 1 gm., magnesium sulphate 0·2 gm. and yeast extract 1 gm. The inoculated medium was incubated for 10 days at 27–28° C. The formation of the trisaccharide was detected by paper chromatography and it was isolated by carbon-column chromatography. The yield was 46 gm. from the culture medium (10 l.).

0·5 gm. of the lactase preparation of *Saccharomyces fragilis*[10] (kindly supplied by Dr. Henry Roberts) and 10 gm. of the trisaccharide were added to 100 ml. of 0·067 *M* phosphate buffer, *p*H 6·2. This solution was incubated at 35° C. for 30 hr. Galactose, kojibiose, a trace of glucose and the trisaccharide were detected by paper chromatography. 5 gm. of kojibiose were isolated by carbon-column chromatography. By acetylation with acetic anhydride and sodium acetate, crystals of the α- and β-octaacetates of kojibiose were obtained. The α-form had m.p. 166° C. (yield 1·7 gm.); the β-form had m.p. 117–118° C. (yield 3·5 gm.). Further, by acetolysis of 10 gm. of the trisaccharide with acetic anhydride (50 ml.), glacial acetic acid (32 ml.) and concentrated sulphuric acid (6 ml.) at room temperature for 7 days, 0·4 gm. of α- and 0·8 gm. of β-kojibiose octaacetates were obtained in crystalline form.

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Origin of the Methoxyl Groups in Spirilloxanthin—a Carotenoid synthesized by the Photosynthetic Bacterium *Rhodospirillum rubrum*

It can now be stated with a reasonable assurance that the repeating (isoprene) unit of all terpenoid compounds arises from two-carbon (acetate) units via mevalonic acid (β,δ-dihydroxy-β-methylvaleric acid) or a closely related compound[1]. Occasionally, however, additional carbon atoms appear the origin of which cannot readily be referred to an isoprene unit; this is most marked in the plant sterols and perhaps the best example is ergosterol with its additional methyl substituent at C_{24}. It has been shown that this group arises by means of the transfer of a one-carbon unit from a donor such as active methionine or formyl- or hydroxymethyl-tetrahydrofolic acid, because formate-^{14}C is readily and specifically incorporated into C_{28} of ergosterol in yeast[2].

The only carotenoids which are known to contain such 'supernumerary' groups are those predominating in the photosynthetic bacteria. These have methoxyl groups attached to either positions 3 and 3′ or 4 and 4′; the best known pigment of this type is spirilloxanthin[3] (Fig. 1), which represents more than 95 per cent of the total carotenoids in mature cultures of *Rhodospirillum rubrum*[4]. Experiments have now been carried out which demonstrate that the methoxyl carbons of spirilloxanthin arise from a one-carbon unit and not from a degraded two-carbon unit.

Young anaerobic cultures of *R. rubrum* contain a mixture of carotenoids, the major components being lycopene, lycoxanthin (3-hydroxylycopene), *P*-481 and hydroxy *P*-481 (pigments of undecided structure but which must be intermediate between lycopene and spirilloxanthin) and spirilloxanthin[4]. If such

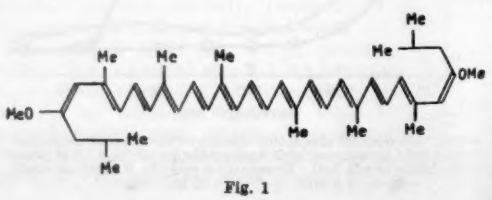

Fig. 1

cultures are washed and resuspended anaerobically in phosphate buffer, additional spirilloxanthin is synthesized while the remaining pigments disappear; the amount of spirilloxanthin formed is stoicheiometrically equivalent to the amount of the other pigments disappearing[5]. These observations strongly suggest that lycopene is converted into spirilloxanthin via *P*-481, etc., as intermediates. If direct methylation occurs during this transformation then addition of a labelled one-carbon compound to washed young cells should yield spirilloxanthin labelled only in the methoxyl groups. Consequently, 36-hr. anaerobic cultures grown under our standard conditions[6] were washed and resuspended anaerobically in the light in *M*/15 phosphate buffer (*p*H 7·0) to which had been added formate-^{14}C. 24 hr. later the cells were harvested, the spirilloxanthin extracted, purified chromatographically[6] and diluted with unlabelled crystalline spirilloxanthin isolated previously from large-scale cultures of *R. rubrum*. The pigment was then recrystallized from benzene to constant specific activity and the methoxyl groups oxidized to methyl iodide using standard micro procedures; the methyl iodide was trapped in freshly distilled quinoline[7]. Approximately 51 per cent of the total activity in the spirilloxanthin was found to be located in the trapped methyl iodide. Allowing for possible losses in the degradation of the pigment and in trapping the methyl iodide, this result leaves no doubt that formate is specifically incorporated into the methoxyl carbons of spirilloxanthin; a random distribution would have yielded less than 5 per cent of the total counts in the methoxyl carbons. Furthermore, the adequacy of the degradation from the isotope point of view was demonstrated by degrading a highly active sample of β-carotene, a carotenoid which contains no methoxyl groups; only 0·16 per cent of the added label was recovered in the quinoline-trapping agent.

Although it has not been possible to demonstrate directly that it is a methyl group rather than a methoxyl group which is transferred, the first possibility is much more likely because (*a*) transmethylation is a well-known and widespread biochemical reaction while transmethoxylation has not yet been reported and (*b*) probable hydroxylated methyl acceptors such as lycoxanthin, hydroxy *P*-481 and 'demethylated' spirilloxanthin[6,8] are present in young *R. rubrum*.

The occurrence of O-methylation in the carotenoids also fits in with the work of Birch *et al.*[9], who found that the methoxyl (and methyl) groups of the benzene ring of mycophenolic acid produced by *Penicillium brevi-compactum* arise similarly by one-carbon transfer, in this particular case from the S-methyl group of methionine.

Only about 25 per cent of the total formate incorporated into the unsaponifiable matter of *R. rubrum* is present in spirilloxanthin. Apart from the carotenoids, the nature of the other unsaponifiable components of *R. rubrum* is unknown but sterols do not appear to be present. It is interesting that formate is rapidly incorporated into this unknown fraction.

A question which still remains to be answered is, why the photosynthetic bacteria methylate their xanthophylls. Xanthophylls are abundant in all other photosynthetic organisms (higher plants and algae) but there is no indication that they are ever methylated[10].

We wish to thank Prof. A. J. Birch for a generous gift of formate-^{14}C and Dr. W. B. Whalley for arranging for the methoxyl determinations to be carried out in the Department of Organic Chemistry of the University of Liverpool.

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Electrophoresis of Fluorescent Antibody

A complication often encountered in the use of the fluorescent antibody technique of Coons and Kaplan[1] is the presence of non-specific staining material in the conjugates, even after exhaustive dialysis. Apart from its nuisance-value, the effect is of interest because it does not occur when fluorescein-globulin reacts with sections of various malignant tissues[2,3].

A number of methods have been suggested for diminishing non-specific staining. Coons and Kaplan[1] used absorption with acetone-dried powders of certain tissues. It has also been found possible to isolate specifically staining fluorescent antibody by absorption to and elution from columns of antigen coupled powdered cellulose (unpublished work). These methods are of uncertain reproducibility, working well with some antibodies and tissues, but not with others. This communication presents some preliminary results of a physico-chemical study on fluorescein-protein conjugates, made in the hope of gaining more information about the chemistry of non-specific staining.

The electrophoresis pattern (Fig. 1) of fluorescein-conjugated human γ_2-globulin (8 μgm. fluorescein/mgm. of protein) shows marked heterogeneity. The spike has a mobility of $-1{\cdot}46 \times 10^{-5}$ sec.$^{-1}$ V.$^{-1}$ cm.^{2} in sodium diethylbarbiturate buffer (*p*H 8·6, *I*, 0·1). A tracing of the ascending boundary of this pattern is superimposed in Fig. 2 on that of normal γ_2-globulin (mobility, $-1{\cdot}01 \times 10^{-5}$ sec.$^{-1}$ V.$^{-1}$ cm.^{2} in sodium diethylbarbiturate buffer, *p*H 8·6, *I*, 0·1).

If the conjugate is shaken with acetone-dried rat liver powder[1] in phosphate buffer (*p*H 7·2, *I*, 0·1) a reduction in the area of the leading peak is observed (Fig. 3). If the γ_2-globulin was prepared from sera of

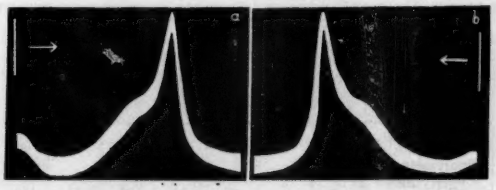

Fig. 1. Electrophoresis of fluorescein-conjugated human γ_2-globulin in sodium diethylbarbiturate buffer (*p*H 8·6, *I* 0·1). *a*, ascending, *b*, descending. The vertical line and arrow indicate origin and direction of migration in each case

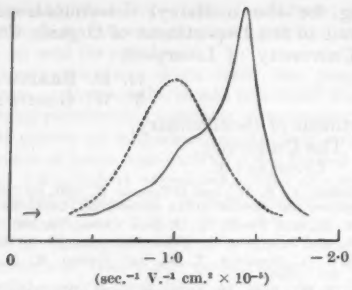

Fig. 2. Tracing of the ascending boundary of Fig. 1 superimposed on that of normal γ_2-globulin (broken line) in sodium diethylbarbiturate buffer (*p*H 8·6, *I* 0·1)

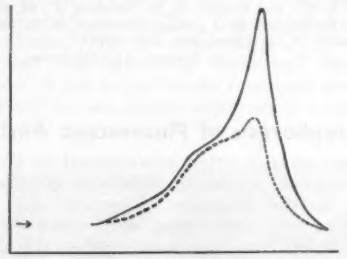

Fig. 3. The ascending electrophoresis pattern of rat liver powder-absorbed fluorescein-rabbit γ_2-globulin superimposed on that of unabsorbed fluorescein globulin (broken line). Electrophoresis in sodium diethylbarbiturate buffer (*p*H 8·6, *I* 0·1)

rabbits hyperimmunized against ovalbumin (domestic fowl) this marked diminution was associated with a loss of only 25 per cent of the antibody activity, as determined by diffusion in agar[4]. In contrast to the unabsorbed conjugates the absorbed material gave very little non-specific staining under the fluorescence microscope when applied to smears of leucocytes from normal human blood.

Attempts at separating the antibody from the non-specific staining activity by electrophoresis with starch blocks and powdered cellulose supporting media proved disappointing. An appreciable portion of the fast non-specifically staining material tailed during the run and was eluted with the antibody fraction.

However, it was possible to fractionate the fluorescein-globulin conjugate by electrophoresis convection. A 3 per cent solution of fluorescein-rabbit γ_2-globulin (containing anti-ovalbumin) was subjected to electrophoresis convection in an apparatus after the design of Raymond[5] at 20 V. cm.$^{-1}$ in six stages in phosphate buffer from *p*H 8·0 to 5·5 (*I*, 0·1), the *p*H being lowered by 0·5 at each stage. The assays of the top fraction from each stage are given in Table 1. It can be seen that the first two stages contain high-titre fluorescent antibody with no non-specific staining properties, and that the last fractions are the most heavily conjugated.

Table 1. Assay of Fluorescein-Globulin Fractions obtained by Electrophoresis-convection

Fraction	1 (*p*H 8·0)	2 (*p*H 7·5)	3 (*p*H 7·0)	4 (*p*H 6·5)	5 (*p*H 6·0)	6 (*p*H 5·5)	Starting material
Protein conc. (mgm./ml.)	2	4	7	7	6	5	30
Fluorescein content (μgm./ml.)	3	8	17	31	63	51	240
Antibody titre	150	430	180	150	100	60	1,024
Non-specific staining	—	—	+	++	+++	+++	+++

These findings present another facet of the well-known heterogeneity of γ-globulin—in this case its heterogeneous chemical reactivity. It is interesting to note that human serum albumin and a relatively homogeneous myeloma globulin both increased in mobility, but only slightly in heterogeneity (estimated by reversible boundary spreading) on conjugation with fluorescein *iso*cyanate.

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Reconstruction of the Reaction Mechanism of Cytochrome Oxidase

Previously it has been generally believed that the substrates of the cytochrome oxidase system, such as *p*-phenylene diamine and hydroquinone, are only oxidized by cytochrome oxidase through cytochrome *c*. However, since *p*-phenylene diamine is fairly well oxidized by particulate cytochrome oxidase preparations in the absence of cytochrome *c*, whereas the other substrates, such as hydroquinone are not, Okunuki[1] has suggested that the reductant of the so-called Nadi-reaction can reduce not only cytochrome *c* but also cytochrome oxidase. This was confirmed spectrophotometrically by Smith[2].

Recently, we reported[3] several properties of our cytochrome *a* preparation and showed that dithionite-reduced cytochrome *a* is oxygenated rather than oxidized by oxygen in the absence of cytochrome *c*. We also showed that in the presence of a small amount of reduced or oxidized cytochrome *c* the oxygenated cytochrome *a* is rapidly oxidized. In this communication the reduction velocity of cytochrome *a* by *p*-phenylene diamine, hydroquinone, and ascorbic acid in a solution of a synthetic non-ionic detergent, 'Emasol' 4130[4] is reported. We also confirm the role of cytochrome *c* in the appearance of the cytochrome oxidase activity of cytochrome *a*.

Cytochrome *a* in 'Emasol' 4130 is readily reduced by the addition of 10^{-3} *M* *p*-phenylene diamine as measured by the change in optical density of the α-band. The velocity measured by the change in the γ-band is somewhat less, due to contamination of the oxygenated form. In contrast to the results of Smith, we find that hydroquinone and ascorbic acid can also reduce cytochrome *a*, though at a slower rate than *p*-phenylene diamine. In an initial 1-min. reaction and at a concentration of 10^{-3} *M* the percentage reduction of cytochrome *a*, measured by the change in its α-band, is 92 for *p*-phenylene diamine, 55 for hydroquinone and 39 for ascorbic acid. When measured manometrically in the absence of cytochrome *c*, none of these substrates caused any uptake of oxygen. However, addition of cytochrome *c* to the cytochrome *a* preparation causes a large oxygen uptake (Table 1).

On the other hand, when a trace of borohydride is added to decrease the concentration of oxygen in the

Table 1. Influence of Addition of Cytochrome *c* on the Cytochrome Oxidase Activity of Cytochrome *a* (Oxygen Uptake/10 min.)

System \ Substrate (10^{-2} *M*)	*p*-Phenylene diamine	Hydroquinone	Ascorbic acid
No addition	4 μl.	4 μl.	10 μl.
Cytochrome *a*	6	4	4
Cytochrome *a* + cytochrome *c* ($1{\cdot}4 \times 10^{-5}$ *M*)	104	126	80

cuvette, cytochrome *a* is oxygenated in aerobic conditions and reduced in anaerobic conditions by the addition of 10^{-4} *M* *p*-phenylene diamine.

When a trace of cytochrome *c* is added to either system, either form of cytochrome *a* is instantaneously oxidized (Fig. 1).

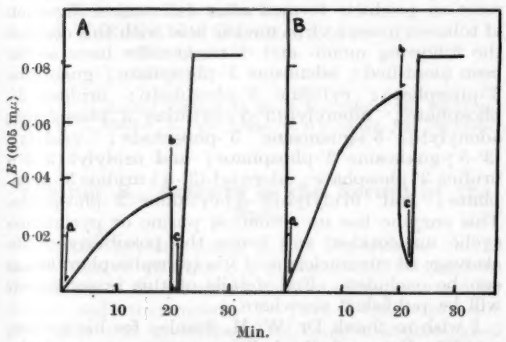

Fig. 1. Effect of cytochrome *c* on the oxidation of cytochrome *a*. Experiments conducted spectrophotometrically in a cuvette of 1 cm. light-path: *A*, cytochrome *a* incubated aerobically; *B*, anaerobically. Arrows indicate addition of each reagent: (*a*) 10^{-4} *M* *p*-phenylene diamine and trace of sodium borohydride; (*b*) 5×10^{-5} *M* of oxidized cytochrome *c*; (*c*) trace of sodium dithionite

Considering these findings in relation to those of Yakushiji and Okunuki[5] that electrons are also transferred from cytochrome *a* to cytochrome *c*, it seems that the electron in the hæm of cytochrome *a* does not participate in the cytochrome oxidase reaction unless cytochrome *c* is present in the system. The following scheme is therefore suggested to illustrate the reaction mechanism of cytochrome oxidase.

Cytochrome oxidase system : O_2 . Cyt.a_r ⇅ Cyt.c → Cyt.c_1 ←

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Preparation of Crystalline *Pseudomonas* Cytochrome$_{551}$ from *Pseudomonas aeruginosa*

Using a strain of *Pseudomonas aeruginosa*, we have already succeeded[1-3] in the purification of four kinds of respiratory components—*Pseudomonas* (*P*-) cytochrome oxidase containing the so-called cytochrome a_2, *P*-cytochrome$_{551}$, *P*-cytochrome$_{554}$ and *P*-blue protein—in forms soluble in water, without the aid of detergents. The crystallization of *P*-blue protein has been described[3]. Here the crystallization of *P*-cytochrome$_{551}$ is reported.

The principle used is as follows. (1) Extraction of the cytochrome from an acetone-powder of the cells. (2) Removal of viscous substances with acidic isoelectric points, such as nucleic acids, by the addition of rivanol. (3) Removal of substances with alkaline isoelectric points by treatment with 'Duolite' *CS*-101, which has similar properties to 'Amberlite' *XE*-64. (4) Rough fractionation of *P*-cytochrome$_{551}$ by chromatography on a column of specially buffered, activated aluminium oxide. (5) Fractionation by zone-electrophoresis on a column of raw potato starch. (6) Precipitation from ammonium sulphate solution, taking advantage of the great difference between the solubilities of the oxidized and reduced forms of the cytochrome.

The partial purification of *P*-cytochrome$_{551}$ by the first four steps has been described[1]. Using the resulting sample, zone-electrophoresis was carried out on a vertical column packed with potato starch (3 cm. in diameter, 30 cm. in height) under the following condition: 0·1 *M* sodium phosphate buffer, *p*H 7·0; current, about 20 m.amp. (350–400 V.); temperature, 4–5° C. The sample was placed in the middle of the column in a concentrated solution. Soon after the beginning of electrophoresis, a lot of brown impurities, not removed by treatment with rivanol, migrated downwards (anode) fairly rapidly, while the *P*-cytochrome$_{551}$ remained near the starting line. After 40 hr., the column was fractionated with the same buffer, using the same method as for normal resin columns. The brown impurities were eluted first and so could be removed easily. Nothing was eluted out after the cytochrome-containing fractions. The fractions of cytochrome were collected and their *E*(red.550·5)/*E*(oxid.275) ratios were found to be higher than 0·90 (this is the ratio of extinction at 550·5 mμ in the dithionite-reduced form to that at 275 mμ in the oxidized form).

The cytochrome collected was then oxidized by addition of the minimum amount of potassium ferricyanide, and precipitated with ammonium sulphate. The precipitate was washed with 80 per cent ammonium sulphate and dissolved in a small amount of distilled water (*E*(red.550·5), 40–60). Solid ammonium sulphate was added to the solution until it became slightly turbid (about 30–35 per cent saturation) and then it was immediately centrifuged. By this procedure, a small part of the cytochrome was precipitated, indicating a suitable concentration of ammonium sulphate for the following procedure. The deep red supernatant was reduced by the addition of a small amount of sodium dithionite, this reduction immediately causing a great increase in turbidity. After the yellowish-red solution had been kept overnight in a refrigerator, it was centrifuged. In most cases, the precipitate consisted of small, but fine needle-like crystals of *P*-cytochrome$_{551}$. The crystalline precipitate was dissolved in a small

Fig. 1. Crystals of *Pseudomonas* cytochrome$_{551}$. (× 800)

amount of distilled water. After the re-addition of a trace of sodium dithionite, solid ammonium sulphate was added to give slight turbidity, with frequent adjustments of the *p*H to 7–8 with ammonia. The solution gradually increased in turbidity and the needle-like crystals shown in Fig. 1 began to appear after a few hours storage. The addition of the ammonium sulphate and the storage should be carried out at almost the same temperature, since the solubility of *P*-cytochrome$_{551}$ in ammonium sulphate solution increases greatly as the temperature decreases.

Twice recrystallized *P*-cytochrome$_{551}$ had the absorption spectrum shown in Fig. 2, and more than two recrystallizations did not increase its purity.

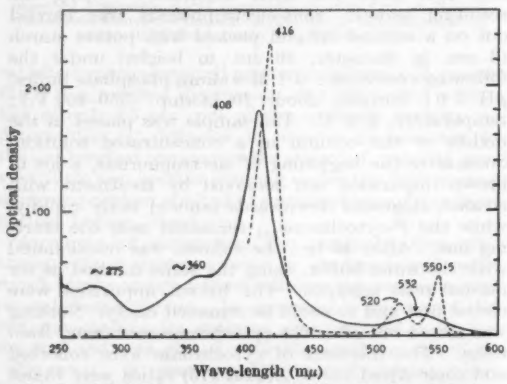

Fig. 2. Absorption spectrum of crystalline *Pseudomonas* cytochrome$_{551}$. ———, Oxidized form; – – –, dithionite-reduced form. The numerals in the figure are the absorption maxima

Compared with crystalline cytochrome *c* prepared from bovine heart muscle[4,5] the α-absorption peak was at a slightly longer wave-length (about 0·5 mμ). The twice recrystallized sample of *P*-cytochrome$_{551}$ was homogeneous both by electrophoresis and by ultracentrifugal analysis.

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Action of Micrococcal Phosphodiesterase on Tobacco Mosaic Virus Nucleic Acid

Cunningham, Catlin and de Garilhe[1] were the first to report the occurrence of a calcium-activated nuclease in the culture medium of *Micrococcus pyogenes* var. *aureus*. These authors partially purified the enzyme and studied its action on deoxyribonucleic acid. In the complete digest they reported the presence of mononucleoside 3′-phosphates and also oligonucleotides. The latter were not identified except for one dinucleotide, deoxyadenylyl-(3′-5′)-deoxycytidine 3′-phosphate[2]. Recently, it was further demonstrated that this enzyme, when activated with calcium, hydrolyses ribonucleic acid[3].

This enzyme has been purified in this laboratory a hundredfold and its action on tobacco mosaic virus nucleic acid was studied. Our enzyme preparations also require calcium ion for activation. Among the reaction products formed after exhaustive digestion of tobacco mosaic virus nucleic acid with this enzyme the following mono- and di-nucleotides have so far been identified: adenosine 3′-phosphate; guanosine 3′-phosphate; cytidine 3′-phosphate; uridine 3′-phosphate; adenylyl-(3′-5′)-cytidine 3′-phosphate; adenylyl-(3′-5′)-guanosine 3′-phosphate; uridylyl-(3′-5′)-guanosine 3′-phosphate; and uridylyl-(3′-5′)-uridine 3′-phosphate; adenylyl-(3′-5′)-uridine 3′-phosphate; and uridylyl-(3′-5′)-cytidine 3′-phosphate. This enzyme has no action on purine or pyrimidine cyclic nucleotides, and hence the possibility of its cleavage of ribonucleic acid via transphosphorylation can be excluded. Full details of this investigation will be published elsewhere.

I wish to thank Dr. W. M. Stanley for his interest and Miss Patrice J. Driskell for supplying me with the organism used in these studies. This investigation was aided by grants from the Rockefeller Foundation and the United States Public Health Service.

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Isolation of $\Delta^{5,7,9}$-Œstratrienol-3-one-17 from the Urine of Pregnant Mares

$\Delta^{5,7,9}$-Œstratrienol-3-one-17 was isolated from pregnant mares' urine in 1940 by Heard and Hoffman[1]. These workers obtained approximately 160 mgm. of pure material per 10,000 gallons of urine, that is, about 3·8 μgm./l., but stated that this did not represent the total quantity excreted. Since no other isolations of $\Delta^{5,7,9}$-œstratrienol-3-one-17 from pregnant mares' urine have been reported in the literature, we believe that it is of interest to record that we have found the material to be present in pregnant mares' urine in relatively large quantities (approximately 430 gm. of $\Delta^{5,7,9}$-œstratrienol-3-one-17 per 10,000 gallons of urine, that is, about 10 mgm./l.) and that we have isolated the material readily in the pure state.

A concentrate, representative of mares' urine collected from approximately the fourth to ninth month of pregnancy, was prepared by methods previously outlined by us[2]. The concentrate was

subjected to hydrolysis and a non-phenolic ketonic fraction isolated which yielded, after acetylation, approximately 100 gm. of pure $\Delta^{5,7,9}$-œstratrienol-3-one-17 acetate on repeated crystallizations. This acetate had the following properties: m.p. 167–69° C.; $\lambda_{max.}$ (alc.) 269 mμ, $\varepsilon = 395$; $\bar{\nu}_{max.}$ (CS_2) 1,736 cm.$^{-1}$ and 1,242 cm.$^{-1}$ (acetate), 810 cm.$^{-1}$ (aromatic ring *B*). The infra-red spectrum was identical with that of a sample of $\Delta^{5,7,9}$-œstratrienolone acetate kindly supplied by the late Prof. R. D. H. Heard. On hydrolysis with perchloric acid in methanol at room temperature an 85 per cent yield of the free alcohol was obtained. This had a melting point of 146–49° C., and had bands in the infra-red (CS_2) at 1,741 cm.$^{-1}$ (17-ketone) and 811 cm.$^{-1}$ (aromatic ring *B*).

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Vitamin B_{12} Activity in the Serum of the Rat

A study is being made in this Department on the metabolism of vitamin B_{12} in the albino rat, and on the effects of deficiency of this vitamin produced by dietary and other means. As part of this study, the possibility was investigated of using microbiological assays of vitamin B_{12} activity in serum to assess the nutritional state of the animals with regard to vitamin B_{12} in the same way as in human subjects. This communication describes preliminary results obtained on normal and gastrectomized rats and on rats which had been kept on a diet deficient in vitamin B_{12}.

Albino rats of the Wistar strain were used. Blood (1–2 ml.) was obtained by cardiac puncture and was allowed to clot in small test-tubes. The clots were broken up with glass rods, the samples were centrifuged, and the serum was removed and stored frozen until required for assay. The vitamin B_{12} activity in the serum was assayed by a method described by one of us[1], using *Lactobacillus leichmannii* as test organism. Owing to the small amounts of serum obtainable from rats, protein-free extracts were prepared from 0·4 ml. portions of serum, and assays were carried out at one dilution only, corresponding to 1 ml. of a 1 : 20 dilution of serum per 5 ml. of assay medium. Tests using larger amounts of pooled serum from various groups of animals showed that the values obtained using different dilutions of serum were the same within the limits of accuracy expected from microbiological assays. The method gave quantitative recoveries of vitamin B_{12} added to pooled rat serum (Table 2).

The results obtained in various groups of animals are shown in Table 1. It is evident that both gastrectomy and dietary deficiency of vitamin B_{12} can cause reduction in the vitamin B_{12} activity of the serum to subnormal levels, so that the estimation seems to be useful in deciding whether or not an animal is deficient in vitamin B_{12}.

The levels in both the normal and the deficient animals, however, are high compared with those found in normal subjects and patients with untreated pernicious anæmia respectively[2]. This appears to be because rat serum contains a substance which has vitamin B_{12} activity for *Lactobacillus leichmannii*, but which is stable to boiling for 30 min. at *p*H 12, a treatment which destroys vitamin B_{12} and almost all the vitamin B_{12} activity in human serum[1]. Table 2 shows the vitamin B_{12} activity of pooled sera from different groups of rats before and after boiling with alkali. While about 50 per cent of the activity in normal rat serum is destroyed, much less is destroyed in serum from gastrectomized rats and rats kept on a diet deficient in vitamin B_{12}. The alkali-stable fraction, however, is roughly the same in all the groups. This suggests that deficiency of vitamin B_{12} causes a gross depletion of true vitamin B_{12}, the alkali-labile fraction, but that the alkali-stable fraction is unaffected. When serum to which vitamin B_{12} has been added is treated with alkali, the activity remaining is virtually the same as that found after treating with alkali the same sample of serum without added vitamin B_{12} (Table 2).

Table 1. Vitamin B_{12} Activity in the Serum of Various Groups of Rats

Group	No. of animals	μμgm. vitamin B_{12} activity per ml. serum	
		Mean	Range
Normal	36	983	630–1,500
Gastrectomized (1–12 months after operation)	6	402	350–480
Animals fed a diet deficient in vitamin B_{12} for 6 months	4	515	460–560
Normal (assayed with *Euglena gracilis*)	6	150	100–180

Table 2. Vitamin B_{12} Activity of Samples of Pooled Rat Serum Before and After Treatment with Alkali

Sample No.	Group of rats	μμgm. vitamin B_{12} activity per ml. serum	
		Before alkali treatment	After alkali treatment
1	Normal	1,400	460
2	Normal	1,200* 1,300*	550* 530*
3	Normal	830* 730*	450* 370*
3 + 1,000 μμgm. vitamin B_{12} per ml. added	Normal	2,000	420
4	Normal	770	460
4 + 1,000 μμgm. vitamin B_{12} per ml. added	Normal	1,900	490
5	Gastrectomized	430	410
6	Fed diet deficient in vitamin B_{12} for 6 months	610	510

* Results of separate assays on the same sample of serum.

Estimations of vitamin B_{12} activity were kindly carried out for us on the sera of 6 rats by Dr. W. M. Davidson of King's College Hospital Medical School, London, using *Euglena gracilis* as test organism. The results are included in Table 1. Although *Euglena* gives lower results than *Lactobacillus leichmannii* on human serum, the difference would not account for the discrepancy found with the rat sera, so that the alkali-stable fraction in rat serum may be inactive for *Euglena*. Experiments are in progress to determine the nature of the alkali-stable fraction.

We are grateful to Mrs. Beryl Godfrey and to Mrs. Elisabeth Ross for assistance with the microbiological assays, and to Prof. L. J. Witts for his interest in the

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Effect of Hydrogen Peroxide on Transplanted Rat and Mouse Tumours

Recently, Holman[1] has reported that daily continued oral administration of commercial hydrogen peroxide (in drinking water) caused complete regression of Walker carcinoma 256 in rats in 50–60 per cent of the cases. This laboratory finding was applied in humans with advanced inoperable cancers. In two of the four cases there was reported a definite subjective and objective improvement[1]. The obvious importance of these findings in the case of a compound so plentiful made it desirable to attempt to confirm these results in Walker carcinoma 256 and in several of other animal tumours.

The tumours used in the present study were sarcoma 180, adenocarcinoma *E* 0771, Mecca lymphosarcoma, sarcoma ascites tumour and Ehrlich ascites carcinoma in mice, and Walker carcinosarcoma 256 in rats. The history, biological properties and cytological description of these tumours are given elsewhere[2].

Subcutaneous implantations of tumours were carried out by the usual trocar method. The progress of the tumours in the treated and the untreated animals was recorded graphically by measuring the diameters of the tumours with calipers at weekly intervals for four weeks after tumour transplantation. In the case of ascites tumours[2], intraperitoneal injection of 0·1 c.c. of the fluid containing about one million cancer cells was made into each mouse in the inguinal region. The animals were maintained on a standard pellet diet (Purina Laboratory Chow).

Animals implanted with various tumours were treated by simply replacing their drinking water with distilled water containing 0·3, 0·45 and 0·9 per cent by weight of hydrogen peroxide (U.S.P.). The dilute solutions of hydrogen peroxide were prepared daily. During the experiment, the drinking water-bottles were covered with a tinfoil. The hydrogen peroxide content of the diluted solutions remained practically unchanged after standing 24 hr. in an air-conditioned animal room. The control animals were given water *ad lib.*

The treatment with hydrogen peroxide was started in most cases 24 hr. after transplantation of the tumour, and treatment was continued for four weeks.

The degree of inhibition of the growth of the solid tumours was graded according to the following scheme :

−, No effect ; tumour growth more than three-quarters the average diameter of the controls.
±, Slight inhibition ; tumour growth from a half to three-quarters the average diameter of the controls.
+, Moderate inhibition ; tumour growth from a quarter to a half the average diameter of the controls.
++, Marked inhibition ; no tumour growth or growth to a quarter the average diameter of the controls.

The degree of ascites tumour growth was graded according to the following scheme :

−, No effect, indicating marked abdominal distention ; the fluid volume increases to three-quarters or more of the controls (16–30 c.c.).
± Slight inhibition, indicating moderate abdominal distention ; the fluid volume increases to about a half the volume of the controls (6–15 c.c.).
+, Moderate inhibition, indicating slight abdominal distention ; the fluid volume increases to about a quarter the volume of the controls (1–5 c.c.).
++, Marked inhibition, indicating no abdominal distention ; no gross ascites.

The results obtained with hydrogen peroxide at various dilutions are summarized below and in Tables 1 and 2. In the tables the average changes in weight in grams of treated over control animals after one week of treatment is recorded. Five or ten animals were used in each test group.

The results of the experiments showed that oral administration of 0·3, 0·45 and 0·9 per cent of hydrogen peroxide in drinking water had no inhibitory effect on the growth of sarcoma 180, adenocarcinoma *E* 0771, Mecca lymphosarcoma and Walker carcinosarcoma 256 in animals. Practically all tumours grew rapidly and killed animals in 2–5 weeks after tumour transplantation. In one experiment the effect of hydrogen peroxide on well-established 12-day-old Walker carcinosarcoma 256 was tested. The results of this experiment showed that daily doses of 0·45 per cent by weight of hydrogen peroxide in drinking water had no inhibitory effect on the

Table 1. Effect of Hydrogen Peroxide in Drinking Water on 1-day-old Mouse and Rat Tumours

Tumour	Hydrogen peroxide content (per cent)	Average hydrogen peroxide water consumed by animal/day (c.c.)	No. of deaths		Average weight change (gm.) treated/controls (1st week)	Results of treatment	
			1st week	2nd week		1st week	2nd week
Sarcoma 180	0·3	3·7	0/10	0/10	+ 2·3/+ 2·2	−	−
Sarcoma 180	0·45	2·1	0/10	1/10	+ 0·9/+ 0·9	−	−
Adenocarcinoma *E* 0771	0·3	2·2	0/10	0/10	+ 0·1/+ 0·5	−	−
Mecca lymphosarcoma	0·3	4·3	0/10	2/10	+ 1·8/+ 1·9	−	−
Walker carcinosarcoma 256	0·45	22	0·10	0/10	+ 2)/+ 34	±	−
Walker carcinosarcoma 256	0·9	8·5	1/10	2/10	+ 3/+ 26	−	−
Walker carcinosarcoma 256 (12-day-old)	0·45	16	0/10	0/10	+ 1/+ 11	−	−

Table 2. Effect of Intraperitoneal Injections of Hydrogen Peroxide on 1-day-old Mouse Ascites Tumours

Tumour	Dose (mgm./kgm./day)	No. of deaths		Average weight change (gm.) treated/controls (1st week)	Results of treatment		
		1st week	2nd week		1 day	10 days	14 days
Ehrlich carcinoma	15	0/5	2/5	+ 6·4/+ 5·7	−	−	−
Ehrlich carcinoma	75	0/5	0/5	+ 3·8/+ 5·7	−	−	−
Ehrlich carcinoma	150	0/5	1/5	+ 3·0/+ 5·7	−	−	−
Sarcoma 180	150	0/5	1/5	+ 2·1/+ 6·8	−	−	−
Sarcoma 180	225	0/5	1/5	− 0·6/+ 6·8	+	+	+

tumour. All treated tumours grew normally. When the rats were given 0·9 per cent hydrogen peroxide in drinking water, they consumed less water, and therefore ingested an amount of hydrogen peroxide equivalent to that which was contained in 0·45 per cent hydrogen peroxide.

During the course of this work, we determined the effect of hydrogen peroxide on the growth of two different types of ascites tumours, namely, sarcoma 180 and Ehrlich carcinoma. Mice with these ascites tumours die in about fourteen days with large amounts of ascitic fluid. The first intraperitoneal injection of hydrogen peroxide solutions was given 24 hr. after intraperitoneal injection of about one million cancer cells, and the treatment was continued for seven days. From the results in Table 2, it is evident that doses less than 150 mgm./kgm./day of hydrogen peroxide had no inhibitory effect on the growth of either sarcoma 180 or Ehrlich ascites tumours. However, a higher dose of 225 mgm./kgm. of hydrogen peroxide had a moderate inhibitory effect on sarcoma 180 ascites tumour. Treatment of the well-established ascites tumours was less effective.

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Incorporation of Carbon-14 Dioxide by Duck Erythrocytes and Reticulocytes *in vitro*

PREVIOUS studies *in vivo* on the incorporation of carbon-14 dioxide from carbonate into rat erythrocytes have demonstrated that this is widespread into globin, hæmatin and ghosts[1]. Some fractions of rat blood rich in reticulocytes can also incorporate carbon dioxide *in vitro*[2].

This communication is concerned with the ability of duck blood rich in reticulocytes to incorporate carbon dioxide *in vitro*.

The blood was obtained in the following way: 30 mgm. phenylhydrazine per kgm. body-weight was dissolved in 10 ml. of saline and administered orally. After 48 hr. about 10 ml. of blood per kgm. body-weight was removed and discarded. After 92 hr. blood rich in reticulocytes was removed for incubation. 50 ml. of heparinized blood (10 mgm. per cent of heparin) was added to a saline solution of penicillin and streptomycin (about 3 mgm. per cent). 200 μc. of $NaH^{14}CO_3$ (1 mc./mmole) dissolved in 5 ml. of an isotonic solution containing 0·4107 gm. per cent of sodium carbonate and sodium chloride, and 0·3 per cent glucose was then added to the mixture. 10-ml. aliquots in 30 ml. vessels were incubated, with slow rotation in an atmosphere of 95 per cent oxygen and 5 per cent carbon dioxide for 20 hr. at 38·5 ± 0·1° C.

Hæmatin, globin stroma, and protoporphyrin were prepared by the method previously described[2], histone and deoxyribonucleic acid according to Allfrey *et al.*[3]. The total carbon content was determined according to Van Slyke *et al.*[4] and its activity was measured by the gas-phase counting method[1,2]. The results are shown in Table 1.

From these results it can be seen that there is considerable fixation of carbon from sodium bicarbonate during incubation of duck blood with sodium bicarbonate.

Table 1

Materials	Stroma	Globin	Hæm	Proto-porphyrin	DNA	Histone
Specific activity (disintegrations/mgm. C/min.)	226	154	45·5	1,430	83	130

Error of experimental results less than 10 per cent

The uptake in our experimental conditions is of the order of a few parts per thousand. Because carbon fixation from sodium bicarbonate in biological systems takes place[5] after dehydration of carbonic acid in equilibrium with HCO_3^-, carboxylation reactions are obviously possible in the red cells of the duck.

The widespread incorporation into all the components of red cells we have analysed, suggests that the first products of carboxylation belong to a pool of substances from which all the substances we examined can be synthesized. They could be those of the Krebs cycle[5].

These first products will have a greater specific activity, since they are less diluted with similar labelled compounds. To these products we ascribe the large value of carbon-14 specific activity found in non-protein fractions of the plasma (800 disintegrations/mgm. carbon/min.) and in a hæmolysed fraction containing none of the substances in Table 1 (1,700 disintegrations/mgm. carbon/min.).

The fact that the specific activity of the protoporphyrin is greater than that of the hæm indicates that the protoporphyrin is mainly newly formed by young red cells *in vitro*[6].

The activity found in the globin shows that carbon dioxide is fixed in amino-acids; our present knowledge suggests that it is previously fixed in some keto-acids by carboxylation reactions, and that amino-acids are then formed by transamination. If this is also true for duck red cells, they will contain transaminases. The activity found in the hæm and in the protoporphyrin shows that carbon dioxide is previously fixed in succinate and/or glycine[7]. The specific activity in the hæm is approximately 30 times lower than in the protoporphyrin. From this it can be deduced that for a hæmoglobin concentration of 15 gm. per cent (that is, for a hæm concentration of 0·7 gm. per cent), approximately 20 mgm. of hæm was synthesized in 20 hr.

Adding iron as gluconate to the blood increased the relative specific activity of the hæm (Table 2), as though iron gluconate catalysed the formation of some hæm precursor or inhibited the synthesis of some amino-acid of the globin.

Activity found in the histone shows that there is a nucleoprotein turnover: this result does not conflict with that of Allfrey *et al.*[3], who found no detectable turnover in similar experiments with glycine-^{15}N, in view of the small glycine content of the histone[8] and the sensitivity of their apparatus. The activity found in the deoxyribonucleic acid could also be due

Table 2

Experiment	Relative specific activity	
	Globin	Hæmatin
A (no Fe^{++} added)	1	0·29
B (Fe^{++} added)	1	0·46

Table 3

Time (hr.)	Specific activity in disintegrations/min./mgm. carbon in			
	Globin	Hæm	Stroma	Protoporphyrin
1·5	38	14	41	3,700
3·0	40	18	54	
6·0	50	19	85	3,350
18·0	53	27	107	2,400

Error of experimental results less than 10 per cent

to a direct fixation of carbon dioxide in the purine ring[9].

The specific activity of the stroma was found to be greater than that of the hæmoglobin. This proves that the activity of the stroma is not due only to the residual hæmoglobin trapped; in effect both the protein and the lipid fractions can incorporate carbon dioxide.

Rate of uptake. Incubation was carried out at 38·5 ± 0·1° C. for 1·5, 3, 6 and 18 hr. in an atmosphere of 95 per cent oxygen and 5 per cent carbon dioxide. Samples of 15 ml. of blood from the same duck were mixed with 60 μc. $NaH^{14}CO_3$ (specific activity 1 mc./mole dissolved in 1·5 ml. of an isotonic solution). 0·7 mgm. of iron as gluconate, 50 mgm. of glucose, 1·25 mgm. each of sodium benzyl-penicillin and dihydrostreptomycin sulphate were also added. The preparation of the materials and the method of measuring the specific activity have already been described[1,2].

The results are shown in Table 3; specific activity values are plotted against incubation time in Fig. 1.

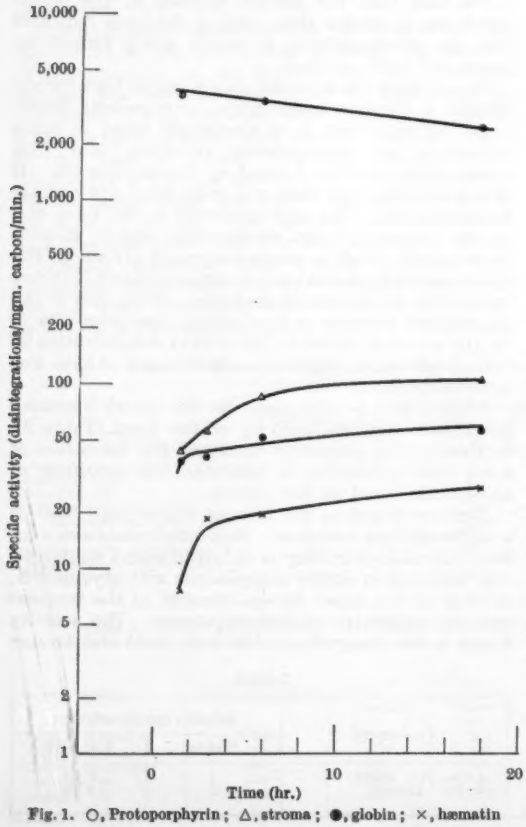

Fig. 1. ○, Protoporphyrin; △, stroma; ●, globin; ×, hæmatin

Carbon incorporation from sodium bicarbonate follows the same pattern, within experimental error, for globin and hæmatin: it can be deduced that the rate of hæmatin and globin synthesis is the same; that is, there is not a different turnover for the two substances. The decreasing rate after the first 4 hr. (in which 70 per cent of newly synthesized hæmoglobin is formed) may be due to a progressive deficiency of amino-acids. Our results on the rate of new synthesis of hæmatin are in good agreement with those reported by Shemin *et al.*[7] on the rate of incorporation of glycine-^{15}N by duck blood in similar experimental conditions.

Carbon uptake from sodium bicarbonate into stroma and into protoporphyrin is different from that seen in hæmoglobin. The specific activity of protoporphyrin decreases slightly with time: this may be due to dilution with less active protoporphyrin arising from the catabolism of the hæmatin.

Further experiments are in progress to extend these results.

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Development of Skeletal Muscle Protein

We have reported determinations of the actin and myosin in the skeletal muscle of a chick 72 [1,2] and 96 [3] hr. after incubation respectively. In order to test whether the appearance of actin in the developing skeletal muscle before the formation of myosin is limited to chick embryos or is a general phenomenon in animals I investigated the formation of actin and myosin in the embryonic stages, and in regenerating limbs after amputation at the knee, of *Triturus pyrrhogaster* using the same methods as before.

G-Actin and myosin were isolated from the skeletal muscle tissue of good-sized specimens of *Triturus pyrrhogaster* by the method of Szent-Györgyi[4]. Both proteins, at a concentration of 25 mgm./ml., were injected intravenously into rabbits at three-day intervals, until they reached a total of 100 mgm. The rabbits were bled by heart puncture on the fifth day after the last injection, and the sera obtained were raised to their serological specificity by resorption tests[5] with saline extracts of liver, spleen and skin tissue of *Triturus pyrrhogaster*. Titration with homologous antigen[6] was then carried out before the precipitin reaction with a saline extract of embryo or granulating tissue of amputated limbs. The titre of both sera was 1 : 512. A possible failure due to excess of antigen was prevented by using a constant

volume of sera and progressively decreasing the amount of antigen.

It was found that actin and myosin first become detectable in the early embryo at stage 19 (about 132 hr. old at 20 ± 1° C.) and stage 24 (about 176 hr. old at 20 ± 1° C.)[7] respectively (Table 1). They were detected in the granula of regenerating limbs about 20 and 27 days after operation (Table 2) respectively, though DeHaan[8] reported a transient appearance of actomyosin in the regenerating limbs of *Amblystoma mexicanum* about 20 days after operation. His result may be due to a cross-reaction of his antisera with developing actin[9].

Table 1. Determination of Developing Skeletal Muscle Protein in Early Embryos of *Triturus pyrrhogaster*

Developmental stages	No. of embryos extracted	No. of reactions series	Lowest antigen concentration to give positive results*	
			Actin	Myosin
18	12	2	—	—
19	12	2	1 : 20	—
20	12	2	1 : 40	—
23	12	2	< 1 : 160	—
24	12	2		1 : 160
25	12	2		< 1 : 160
26	10	2		< 1 : 160
Control (non-fertilized)	24	2	—	—

* Antigen concentrations used ranged from 1 : 10 to 1 : 160 in embryos weight.

Table 2. Determination of Developing Muscle Protein in Regenerating Limb of *Triturus pyrrhogaster*

Days after operation	No. of granules extracted	No. of reactions series	Lowest antigen concentration to give positive results*	
			Actin	Myosin
18	10	2	—	—
20	10	2	1 : 20	—
22	10	2	1 : 160	—
25	10	2	< 1 : 160	—
27	10	2		1 : 10
29	6	2		1 : 40
31	6	2		1 : 160

* Antigen concentrations used ranged from 1 : 10 to 1 : 160 in tissue weight.

Therefore, it is probably generally true that in the skeletal muscle actin appears before the formation of myosin, both in the early stages of development and in regenerating tissue. On the other hand, in the heart muscle of early embryos, myosin appears before actin[1,2,10]. In view of this, the morphological and physiological characteristic differences between heart and skeletal muscle should be examined.

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Fungitoxic Action of 8-Hydroxyquinoline, Pyridine-N-oxide-2-thiol and Sodium Dialkyldithiocarbamates, and their Copper Complexes

In a previous communication[1] on the mode of fungitoxic action on *Aspergillus niger*, we found that of the copper complexes of 8-hydroxyquinoline (oxine) and pyridine-N-oxide-2-thiol (PTO), the 1 : 2 complexes are toxic, but of the sodium dimethyldithiocarbamates (NaDDC) the 1 : 1 complex is toxic but 1 : 2 complex is not. We suggested that this discrepancy is not fundamental but can be explained simply by the difference in solubility of the complexes (Table 1). This hypothesis can now be substantiated by observations on the fungitoxic action on *Glomerella cingulata*, a more sensitive mould than *A. niger*. The experiments were carried out as described before[1], in shaken flasks with a basal medium of glass-distilled water and analytical grade reagents, the total copper content not exceeding the equivalent of 0·01 p.p.m. $CuSO_4.5H_2O$. We found that, unlike *A. niger*, *Glomerella cingulata* does not show 'inversion growth' with sodium dimethyldithiocarbamate and copper and, as could be expected on this ground, it is inhibited by copper dimethyldithiocarbamate ($CuDDC_2$) (Table 1). The toxic concentration of copper dimethyldithiocarbamate appeared to be somewhat higher than the concentration of a saturated solution[2], but this can be easily understood since the dissolution is a rather slow process. From Table 1 it follows that for all three 1 : 2 complexes *G. cingulata* is more sensitive than *A. niger*.

The fact that *G. cingulata* is inhibited by copper dimethyldithiocarbamate suggested that for this mould the inhibition pattern for sodium dimethyldithiocarbamate might be the same as for oxine and pyridine-N-oxide-2-thiol. The experimental results summarized in Table 2 lend support to this hypothesis. Moreover, from the known stability constants[3] and the solubility[2] of copper dimethylthiocarbamate, it is easy to calculate, the amounts of the 1 : 1 and 1 : 2 complexes present in each instance. The results were the same as those obtained earlier[1] with *A. niger* for 8-hydroxyquinoline and pyridine-N-

Table 1. Solubility and Toxicity of the 1 : 2 Complexes of Copper

	Solubility in water (p.p.m.)	Minimum inhibiting conc. (p.p.m.)	
		A. niger	*G. cingulata*
$CuDDC_2$	0·01	no inhibition	0·05
$Cuox_2$	1	0·1	0·02–0·05
$CuPTO_2$	0·2	0·2	0·1

Table 2. Effect of Addition of Copper Sulphate on Growth Inhibition of *Glomerella cingulata* by Sodium Dimethyldithiocarbamate, Oxine Sulphate and Pyridine-N-oxide-2-thiol

$CuSO_4.5H_2O$ (p.p.m.)	Minimum inhibiting conc. (p.p.m.)		
	NaDDC	Oxine sulphate	PTO
0*	0·1	0·02	0·5
0·03	0·05	0·01–0·02	0·1
0·1	0·1	0·02	0·2
0·3	0·1	0·02	0·5
1	0·2	0·05	0·5
3	0·2	0·1	0·5

* Copper content not exceeding the equivalent of 0·01 p.p.m. $CuSO_4.5H_2O$.

Table 3. Effect of the Addition of Copper Sulphate on Growth Inhibition of *Glomerella cingulata* by Sodium Diethyldithiocarbamate (Shake Culture)

$CuSO_4.5H_2O$ (p.p.m.)	Sodium diethyldithiocarbamate (p.p.m.) 0	0·1	0·2	0·5	1	2	5	10	20	50
0*	+	±	±	+	+	+	+	±	−	−
0·1	+	+	±	±	+	+	+	+	−	−
0·3	+	+	−	−	+	+	+	+	−	−
1	+	+	−	−	−	−	±	±	±	−
10	+	+	−	−	−	−	−	−	±	−

* Copper content not exceeding the equivalent of 0·01 p.p.m. of $CuSO_4.5H_2O$.

oxide-2-thiol, namely, the toxicity is determined by the concentration of dissolved 1 : 2 complex, provided that an excess of copper is present in the medium in order that the 1 : 1 complex can be formed as well.

When no copper is added, toxicity is still rather high. This may be due to traces still present in the medium. When, however, all copper is bound by addition of 0·3–1 p.p.m. of sodium dibutyldithiocarbamate—a non-toxic agent with stronger chelating properties than the dimethyl compound, 8-hydroxyquinoline or pyridine-N-oxide-2-thiol—the minimal toxic concentrations of these compounds are 20, 5 and 5 p.p.m. respectively. These figures were not lowered by the addition of even fairly large amounts of ferrous sulphate (10–100 p.p.m.). Thus we must conclude that in contrast to the work of Albert and co-workers[4] with bacteria, the iron complexes are not toxic for moulds, as has also been found for 8-hydroxyquinoline by Anderson and Swaby[5].

We have also found that the fungitoxic action of homologues of sodium dimethyldithiocarbamate is determined in a similar way by the solubility of their 1 : 2 complexes with copper and the sensitivity of the test mould. For *G. cingulata* the inhibition pattern of sodium diethyldithiocarbamate (Table 3) is different from that of the dimethyl compound, but equals it for *A. niger*. This is easily understood from the finding that the solubility of the 1 : 2 complex of copper and diethyldithiocarbamate is far less than that of copper dimethyldithiocarbamate, namely, about 0·002 p.p.m.[2]. While the latter is still sufficiently soluble to inhibit *G. cingulata*, the former is not. Consequently, if sufficient copper is added to the medium, we find a zone of inversion growth (1 : 2 complex) and, at lower sodium diethyldithiocarbamate concentrations, a first zone of inhibition (1 : 1 complex). A second zone of inhibition is caused by the free dithiocarbamate (50 p.p.m.), as is the case with dimethyldithiocarbamate.

Thus a difference in toxicity of the 1 : 2 complexes of the methyl and ethyl compounds is found with *G. cingulata*. A difference in the toxic effect of the 1 : 1 complexes can be clearly seen from experiments with *A. niger*. Whereas sodium dimethyldithiocarbamate always shows a distinct first zone of inhibition in the presence of 10 p.p.m. copper sulphate due to formation of the 1 : 1 complex, no inhibition is seen when the diethyl compound is used instead.

This difference does not necessarily point to the diethyl 1 : 1 complex being less active as compared with the dimethyl 1 : 1 complex, for it is clear that a decrease in solubility of the 1 : 2 complex will cause a lower concentration of 1 : 1 complex in solutions of comparable composition.

When the dipropyl derivative is used, the amount of 1 : 1 complex present is much less again than with the diethyl compound. With *G. cingulata* the 1 : 1 complex causes only some incomplete inhibition at 0·5–10 p.p.m. of sodium dimethyldithiocarbamate, when 10 p.p.m. of copper sulphate is used in the medium. The free dithiocarbamate itself appears to be harmless, even at 200 p.p.m. With the dibutyl derivative there is no inhibition up to 500 p.p.m.

In conclusion, we may say that in the concentration range below 50 p.p.m. the inhibition pattern of the dithiocarbamates is determined by the solubility of the 1 : 2 complex with copper, and the sensitivity of the mould.

We thank Prof. G. J. M. van der Kerk for his interest in this work and for his permission to publish these results.

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Chromatography of Thiol Compounds

The extreme ease of oxidation of the thiol group has hindered the chromatographic separation of mercaptans. Hanes, Hird and Isherwood[1] overcame this difficulty by combining the thiol group with N-ethyl maleimide before chromatographic separation. Cysteine and glutathione were separated in this way and detected by spraying the developed papers with ninhydrin. This spray is not specific for mercaptans, however, and Price and Campbell[2] expanded the technique by condensing the mercaptans with N-(4-hydroxy-1-naphthyl) *iso*maleimide and, after chromatographic separation, detecting the naphthyl derivative by spraying with tetra-azotized di-*o*-anisidine.

The preparation of N-(4-hydroxy-1-naphthyl) *iso*-maleimide by the method of Tsou, Barnett and Seligman[3] is a two-step procedure, and it was found that the overall yield in the synthesis was low. Hence, a more readily available thiol-condensing compound was sought.

The most promising compound of those tried was mercuric chloride. The formation of a mercury complex with the thiol group protected it from oxidation during the chromatographic separation. Furthermore, the introduction of a mercury atom into the compound made the detection of the thiols relatively easy, since the organo-mercury compound reacted with alkaline dithizone (diphenylthio-carbazone).

Between 2 and 3 gm. of plant material was ground in a mortar at room temperature with 10–20 ml. of the mercuric chloride reagent (0·1 per cent mercuric chloride in 40 per cent ethanol and buffered at *p*H 4·0 with *M*/5 acetate buffer). Buffering of the reagent was necessary to obtain consistent results from the subsequent chromatography. The insoluble solid was centrifuged away, the clear filtrate was evaporated to dryness *in vacuo*, and the residue was dissolved in the minimum quantity of 40 per cent ethanol for chroma-

tography. Excess mercuric chloride in the extracting solvent was essential to ensure complete protection of the thiol group from oxidation. After applying the solution to the Whatman No. 4 chromatography paper, the papers were developed in the descending direction using *tert*-butanol/acetic acid/water (4:1:1 v/v) solvent. Alkaline solvents were found to be completely unsatisfactory. Developing the papers in the butanol solvent for 18 hr. at 25° C. resulted in an identifiable separation of cysteine and glutathione, the cysteine having the greater R_F value.

Detection of the organo-mercuric compounds was achieved by spraying the paper with a solution of dithizone (0·03 per cent) in 0·1 *N* ammonium hydroxide followed by gentle warming. The compounds appeared as discrete salmon-pink spots after drying. This colour was stable only for a day or two in the light but for up to three months in the dark. 10 μgm. glutathione was detectable by this procedure.

The reaction between the thiol group and mercuric chloride appears to be partially dependent on the overall structure of the molecule. Neither *o*-thiobenzoic acid nor 2-thio-ethanol react under the conditions specified, but 2-thio-succinic acid, cysteine, cysteic acid and glutathione react readily. This suggests that the position in the carboxyl group in the molecule is also important in the formation of the complex.

Using this technique the presence of mercaptans other than glutathione and cysteine has been detected in dormant plant seeds. Further details of these results will be published later.

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Micro-electrophoresis

I SHOULD like to correct the reference to a publication from our laboratory[1] which appears in a recent article[2] entitled "An Apparatus for Micro-electrophoresis of Small Particles". In Table 1 of that article, a value of 1·31 ± 0·02 μ/sec./V./cm. is quoted as the electrophoretic mobility of human erythrocytes obtained with our apparatus. In our paper we stated: "The cell was calibrated using a suspension of human red blood cells, the mobility of which in *M*/15 phosphate buffer solution at *p*H 7·35 is 1·31 ± 0·02 microns/sec./V./cm.". This is the value obtained by Abramson[3] in an extensive study of the mobilities of mammalian blood cells.

Using the rectangular cells, constructed by fusing two optical flats a distance 0·5 mm. apart, it has so far been impossible to measure accurately the cross-sectional area (*A*) of the cell[4,5]. This is necessary for any absolute determination of mobility values, since the field strength (*X*) is determined from the equation $X = I/kA$, where *I* is the current in amperes and *k* the specific conductance of the dispersion. The cross-sectional area of rectangular cells constructed by cementing glass slides[6] can be measured directly, since the sides are square. The use of such cells has, however, been criticized on the grounds that the use of cement makes cleaning difficult and the unevenness of the surface interferes with the hydrodynamic behaviour of the liquid.

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We apologize to Dr. A. M. James for having misinterpreted the text of the paper by D. E. E. Loveday and him, with reference to the mobility of human erythrocytes in phosphate buffer at a *p*H of 7·4. We were under the impression that this was an actual experimental value.

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Effect of Hydrocortisone on Mitochondrial Membrane Permeability

HYDROCORTISONE has been found to inhibit severely oxidative metabolism *in vitro* by normal rat liver mitochondria. Concentrations of 5×10^{-4} *M* and greater inhibit the oxidation of octanoate, L-glutamate and all tricarboxylic acid cycle intermediates except succinate. Similar patterns of inhibition have been reported for other steroids[1–6].

The hydrocortisone used in this study was a purified sample free from metallic contamination. The steroid was dissolved in a minimal volume of re-distilled ethanol and diluted with water to the required concentration. Ethanol controls were included in each experiment.

Failure to inhibit succinate alone of the tricarboxylic acid substrate oxidations indicated that the mechanism of inhibition might involve pyridine nucleotides which are not present in the succinoxidase system. Reversal of the inhibitions could be achieved by addition of the appropriate coenzyme, nicotinamide and reduced glutathione, to the oxidizing system. This suggested either that hydrocortisone interfered with the function of the respiratory co-factors by competition, inactivation or complex formation or that the steroid acted directly on the mitochondrial membrane. Increased permeability of the mitochondrial membranes could lead to the inactivation of pyridine nucleotide-dependent dehydrogenases by loss of the soluble co-factors. 'Ageing' of enzyme preparations has this effect, as has the hepato-toxin carbon tetrachloride[7,8].

Evidence has been presented that steroids can in fact complex with nucleotides[9,10]. However, the present study shows that complex formation is not the inhibitory mechanism.

The activity of pyridine nucleotide-dependent enzymes may be followed spectrophotometrically by measuring the rate of reduction of the nucleotide, which in the reduced state absorbs light strongly at 340 mμ. The rate of substrate oxidation and linked nucleotide reduction by intact mitochondria is proportional to the permeability of the mitochondrial

membrane to the passage of nucleotide and substrate which are added externally. Permeability of the membrane may thus be measured by the rate of reduction of nucleotide.

Fig. 1 shows clearly that hydrocortisone greatly increases the rate of reduction of diphosphopyridine nucleotide by intact mitochondria oxidizing L-malate. The increased optical density is neither due to absorption by the steroid nor to reduction of diphosphopyridine nucleotide in a reaction involving hydrocortisone.

Elimination of the semipermeable membrane barriers by suspension of the mitochondria in water instead of 0·25 *M* sucrose abolishes the effect of hydrocortisone (Fig. 2). The steroid neither accelerates nor inhibits the reduction of diphosphopyridine nucleotide under these conditions.

Comparison of the rates of reduction of diphosphopyridine nucleotide in Figs. 1 and 2, with allowance for the addition of twice as much enzyme in Fig. 1, shows that hydrocortisone increases the permeability of mitochondrial membranes to the same extent as suspension of the particles in water. Semipermeability is abolished.

It is thus clearly established that inhibition of oxidative metabolism *in vitro* by hydrocortisone is secondary to the action of the steroid in increasing the permeability of mitochondrial membranes. Loss of selective permeability allows the soluble co-factors of respiration to be leached from the mitochondria, inactivating pyridine nucleotide-linked dehydrogenases unless the lost co-factors are added in excess to the oxidizing system.

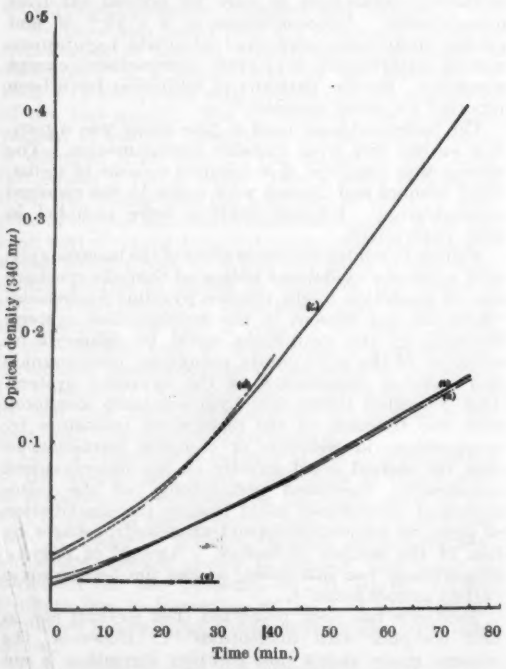

Fig. 1. Reduction of diphosphopyridine nucleotide by liver mitochondria in 0·25 *M* sucrose. (*a*) L-Malate, 0·01 *M*; (*b*) L-malate; 0·01 *M* and ethanol; (*c*) L-malate, 0·01 *M* and hydrocortisone, 0·001 *M*; (*d*) L-malate, 0·01 *M* and hydrocortisone, 0·0005 *M*; (*e*) hydrocortisone, 0·001 *M*. System: sodium–potassium phosphate buffer, *p*H 7·8, 0·033 *M*; potassium chloride, 0·025 *M*; magnesium sulphate, 0·0067 *M*; potassium cyanide, 0·0002 *M*; semicarbazide hydrochloride (neutralized), 0·17 *M*; diphosphopyridine nucleotide, 3 mgm.; enzyme, 50 μl. 1 per cent mitochondria (rat liver) in 0·25 *M* sucrose; water to final volume, 3 ml.; gas phase, air; temperature, 22° C.

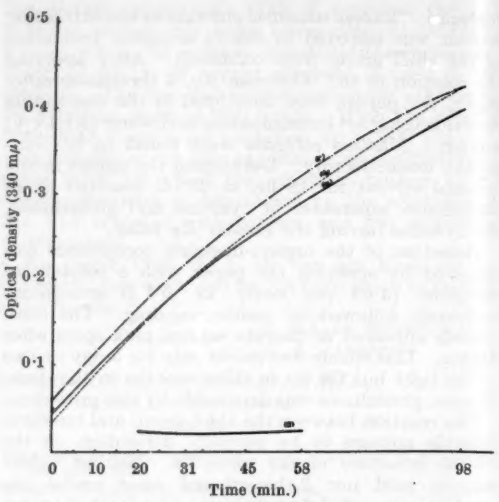

Fig. 2. Reduction of diphosphopyridine nucleotide by liver mitochondria in water. (*a*), (*b*) and (*c*), as Fig. 1; (*d*) hydrocortisone, 0·001 *M*. System: as Fig. 1, enzyme, 50 μl. 0·5 per cent mitochondria (rat liver) in water

This study is reported in detail and the significance discussed in a paper to be submitted to the *Biochemical Journal*.

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Effect of Ethylenediamine Tetraacetic Acid on the Enzyme System of Yeast Cells

The peculiar property of amino-carboxylic acids like ethylenediamine tetraacetic acid of combining with metallic ions forming stable chelate complexes is now established, and has led to the varied uses of this acid in different industries, such as textiles, paper, leather, etc.[1,2]. Under a programme of investigation of the possible use of ethylenediamine tetraacetic acid in the sugar industry, it has been found that the sugar salt complexes responsible for the formation of molasses, and for the loss of appreciable amounts of sucrose in the sugar manufacturing process, could be broken by this acid, releasing the sugar molecules into the free condition; this led to a higher recovery of sugar[3]. During a series of experiments to investigate the possible use of ethylenediamine tetraacetic

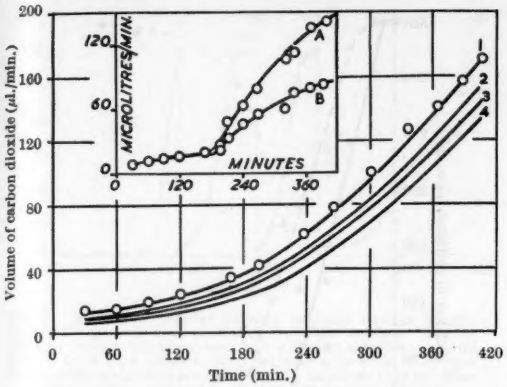

Fig. 1. Time-variation of the rate of evolution of carbon dioxide in the synthetic medium inoculated with yeast cells treated and untreated with ethylenediamine tetraacetic acid. Curves: (1) Yeast cells untreated; (2) treated with 1 per cent ethylenediamine tetraacetic acid for 4 hr.; (3) for 10 hr.; and (4) for 14 hr.

Inset: Curves refer to yeast cells treated with (*A*) 2·5 per cent and (*B*) 5 per cent ethylenediamine tetraacetic acid for 10 hr.

acid for enhancing the yield in the alcohol industry, a few interesting results have been obtained on the effect of the acid on the enzyme system of yeast cells (*Saccharomyces cerevisiae*).

Different samples of molasses obtained from the factories were diluted to 20° Brix; a portion (*A*) of the solution was mixed with the desired quantity (usually 0·25 per cent) of ethylenediamine tetraacetic acid; and the other (*B*) was treated as blank. *A* and *B* were inoculated with yeast and fermented at 30·0 ± 0·1° C. for 72 hr. The amount of alcohol produced, carbon dioxide evolved and yeast formed were estimated by the usual methods. The reducing matter and sucrose content before and after inversion were determined by Somogyi's method[4] which was found by initial experimentation not to be affected by the presence of ethylenediamine tetraacetic acid[5]. Similar experiments were carried out with synthetic media prepared according to White and Munns[6]. In accord with earlier observations[3,5], increased reducing matter and sucrose content were detected in *A*, that is, in the molasses samples and the synthetic media treated with the acid. It is interesting to note that the alcohol formed, carbon dioxide evolved and the yeast produced are markedly less in *A* than in *B*. Thus in one series of experiments, these were respectively 2·23, 6·02, 1·29 gm. in *B* and 2·16, 5·6 and 1·27 in *A*. This difference noted in *A* and *B* is much beyond the experimental accuracy of the methods of analysis. Remarkably enough the amount of sugar consumed during fermentation by yeast in *A* was 7·56 gm. while in *B* it was 6·5 gm. These results indicate that in samples treated with ethylenediamine tetraacetic acid the yeast, while consuming more sugar, gives less ethyl alcohol and carbon dioxide, and suggest that the yeast cells are apparently affected by the acid. This was substantiated by the experiments in which the blank samples of synthetic media *B* were inoculated by yeast which was pretreated with ethylenediamine tetraacetic acid as follows. Well washed yeast cells were suspended in solutions of different concentrations of the acid (in acetate buffer) for varied time-intervals at 5·0° C. and then centrifuged and washed thoroughly. The fermentation was followed up by using Warburg's respirometer. Fig. 1 gives a typical set of results obtained with synthetic media. It may be noted that the amount of carbon dioxide produced decreased markedly with the samples of yeast which were immersed in ethylenediamine tetraacetic acid solution for some time (inset Fig. 1). This is contrary to the favourable effect of the acid noted in the succinic dehydrogenase cytochrome system[7], adenosine triphosphatase[7], papain[8], etc.

Our thanks are due to Prof. S. N. Gundu Rao, director, for his interest and to Dr. N. A. Ramaiah, physical chemist, National Sugar Institute, for helpful discussions.

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A Plate Method for estimating the Numbers of Phosphate-dissolving and Acid-producing Bacteria in Soil

In the past, the preparation of plates for detecting phosphate-dissolving bacteria in soil has involved precipitation of the insoluble phosphate in the medium[1–3]. This method is not very suitable for use with the dilution-plate counting technique. For this purpose we have adapted and extended the suggestion of Johnson[4] in which finely divided dicalcium phosphate is incorporated in agar medium. Other forms of insoluble phosphates can also be used as well as insoluble carbonates. We have used calcium carbonate in this connexion for detecting and estimating acid-producing organisms in soil. Stock suspensions of the insoluble substances are prepared by grinding them in a ball-mill in the presence of gum arabic. The latter is necessary to prevent clumping of the finely divided substances during autoclaving.

Stock suspensions of dicalcium phosphate and calcium carbonate are made up at 2·5 per cent (w/v) and 1·5 per cent (w/v) respectively in 0·5 per cent (w/v) gum arabic. After grinding, they are adjusted to *p*H 8·4 before autoclaving and when afterwards added to molten agar medium the suspensions give uniform plates of a satisfactory and similar opacity. For preparation of the plates 1 ml. of the required suspension is added aseptically to 9 ml. of medium held at 45°. For soil counts we have used a modification of Bunt and Rovira's medium[5], containing 0·5 per cent glucose, in which the diammonium hydrogen phosphate is replaced by 0·05 per cent ammonium sulphate and the *p*H adjusted to 6·8. After thoroughly mixing, by hand rolling, the medium containing the dispersed insoluble compound is poured into Petri dishes already containing the 1-ml. aliquot from the appropriate soil dilution flasks. The insoluble compounds in the final plates when examined by X-ray analysis are found to be chemically unchanged. The plates are incubated at 25° C. for 14 days and the total number of colonies

Table 1

Soil	Dicalcium phosphate dissolving organisms (per cent)	Calcium carbonate dissolving organisms (per cent)
Garden	17·9	48·2
Field	16·2	44·7

and those showing halo production counted. Table 1 gives the results obtained from a field and garden soil.

It can be seen that there is a much higher percentage of acid-producing than phosphate-dissolving organisms, showing that not all acid producers can dissolve insoluble phosphates in soil. Increasing the calcium carbonate to the same concentration as the dicalcium phosphate in the plates (0·25 per cent) did not affect this result. Other forms of insoluble inorganic phosphates tried included freshly precipitated hydroxy-apatite as prepared by Sperber[3]. This did not give as high counts as were obtained with dicalcium phosphate.

It should be mentioned that the technique probably gives an under-estimate of the total numbers of phosphate-dissolving organisms in soil as it is too insensitive to detect those dissolving very small amounts. However, when a comparative study of a large number of soils is required the method has been found to be very convenient. Full details of the results obtained with it and other work on bacteria dissolving phosphate will be published elsewhere.

We are grateful to Mr. W. A. Mitchell of this Institute for carrying out the X-ray analyses.

One of us (H. A. L.) wishes to make acknowledgment to the South African Department of Agriculture and the South African Wheat Industry Control Board for financial support.

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Aerobic Transformation of Cysteine to Sulphate in Soil

Much of the sulphur in soils under pasture in humid and semi-arid regions is in the organic form[1,2], and plants are largely dependent on the conversion of this sulphur to sulphate for their nutrition. At the present time little information is available regarding this transformation in soil. Studies conducted with pure cultures of various soil micro-organisms suggest that, under aerobic conditions, sulphate, sulphur, or hydrogen sulphide may be end-products in the decomposition of organic sulphur compounds. Excellent reviews of this work have been published[3,4].

In order to gain information of the reaction sequence carried out by the mixed flora of a typical 'humid' soil, the oxidation of cysteine was observed using a perfusion unit of the type described by Lees and Quastel[5].

A 0·01 *M* solution of cysteine was perfused through 30 gm. of soil held in the perfusion unit, and samples were removed for qualitative paper chromatographic analysis at two-hourly intervals over a period of three days. Oxidation of the cysteine during chromatography was prevented by the use of N-ethyl-maleimide. The amount of cysteine and cystine in the perfusate was determined quantitatively by the method described by Snell and Snell[6].

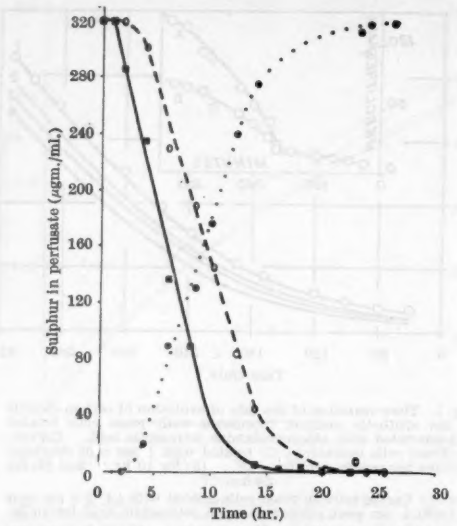

Fig. 1. Conversion of cysteine to cystine in perfusion unit. – – –, Disappearance of cysteine sulphur; . . . ., cystine sulphur production; ——, disappearance of cysteine sulphur from solution 0·01 *M* with respect to azide

Cystine and cystine disulphoxide were positively identified on the chromatograms. Taurine was not detected. The identity of cystine disulphoxide was established by co-chromatography of aliquots of the perfusate with the authentic chemical in a number of solvent systems.

The conversion of cysteine to cystine took place rapidly (Fig. 1). In the presence of azide the conversion was somewhat more rapid than when azide was not added. The acceleration of this reaction in the presence of azide is not explained, but the fact that it proceeds under these conditions suggests that it is non-biological. Cysteine did not appear to be reformed from cystine, as it could not be detected in the perfusate by paper chromatography after the first twenty-four hours.

30 gm. of soil were enriched with micro-organisms carrying out the oxidation of cysteine to sulphate by perfusion with 200 ml. of 0·01 *M* cysteine. When sulphate production was plotted against time, a curve with the typical lag phase of proliferating organisms was obtained (Fig. 2*A*). The system was then freed from sulphate by washing with distilled water, and solutions of possible intermediates re-perfused through the enriched soil, and sulphate production again measured.

When cystine and cystine disulphoxide were perfused through an enriched soil, their sulphate production rate curves did not show the lag phase exhibited by cysteine when it was perfused through fresh soil (Fig. 2). Again, when solutions of these compounds were perfused through fresh soil, the sulphate production rate curves were similar to that obtained for cysteine (Fig. 2*A*). It appears that the population present in the enriched soil was capable of oxidizing cystine and cystine disulphoxide to sulphate, and that these two compounds are indeed

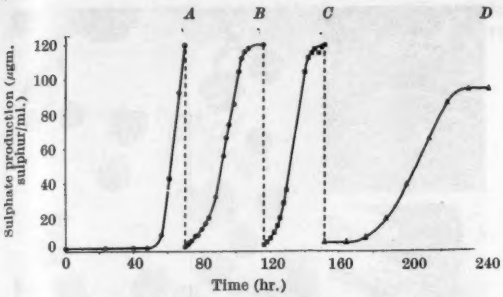

Fig. 2. *A*, 0·01 *M* cysteine solution perfused through 30 gm. fresh soil; *B*, soil from *A* washed free from sulphate then re-perfused with 0·002 *M* cystine hydrochloride solution; *C*, soil from *B* freed from sulphate then perfused with 0·002 *M* cystine disulphoxide hydrochloride solution; *D*, soil from *C* freed from sulphate then perfused with 0·004 *M* taurine solution

intermediates in the transformation of cysteine to sulphate.

Taurine, however, which could not be detected in the perfusate by paper chromatography, was not immediately oxidized to sulphate when perfused through an enriched soil (Fig. 2*D*).

The results obtained here indicate that the transformation of cysteine to sulphate in soil follows the sequence: cysteine→cystine→cystine disulphoxide→cysteine sulphinic acid→sulphate. Although cysteine sulphenic acid has been suggested as an intermediate in the production of sulphate in animal metabolism[7-9], in our system, if it is formed, it would be derived from cystine disulphoxide and not directly from cysteine.

Part of the work reported here was carried out at the Kearney Foundation of Soil Science, University of California, Berkeley, during the tenure of a Commonwealth Scientific and Industrial Research Organization (Australia) Studentship.

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Effect of Gibberellic Acid on the Nodulation of White Clover (*Trifolium repens* L.)

In a recent communication, Thurber, Douglas and Galston[1] reported that spraying of dwarf beans (*Phaseolus vulgaris*) with potassium gibberellate greatly decreased nodulation and they indicated the need for caution in the application of gibberellins to leguminous plants. Probably the most widely used legume in Britain is white clover (*Trifolium repens*), and it is therefore of interest to note the effect of gibberellic acid. on the nodulation of this plant.

Table 1

	No. of nodules per plant
Control	11
Gibberellic acid incorporated in agar and added gibberellic acid	11
Added gibberellic acid only	10

Experiments were carried out in both agar and in soil culture. The nitrogen-free agar culture technique was that previously described[2], there being one plant per tube. Ten tubes were set up with 20 p.p.m. gibberellic acid incorporated in the agar-rooting medium and a further 1 ml. of 20 p.p.m. solution added when the seedlings were transplanted; ten more tubes containing the ordinary agar-rooting medium had 1 ml. of 20 p.p.m. gibberellic acid solution added at transplanting; and there were ten control tubes with no gibberellic acid. The plants were allowed to grow for ten weeks in a cool greenhouse and then harvested. That the gibberellic acid was active was shown by the typical effects on the plant, namely, marked elongation of the hypocotyl and leaf petiole.

In the soil experiment, the clover plants were grown from seed in 3½-in. pots, each pot containing 230 gm. of John Innes compost. Each pot of soil was inoculated with 1·25 ml. of a suspension of *Rhizobium trifolii* (strain 157) containing approximately 260 million bacteria per ml. When the plants had reached the two-leaf stage they were thinned to eight plants per pot. At the three-leaf stage 15 pots of plants were sprayed to dripping point with a solution of 50 p.p.m. gibberellic acid containing 0·1 per cent 'Tween 80' as a spreader. A further 15 pots of plants were sprayed with water containing 0·1 per cent 'Tween 80' as controls. The treatments were repeated ten days later. The plants were harvested sixteen days after the last treatment, by which time the control plants had reached the 10–12 leaf stage. The treated plants were showing a marked increase in petiole length and in leaf area, but a reduction in leaf number to 5 or 6 leaves per plant. The nodules were counted and their dry weights determined. Each reading is the mean of 120 plants.

All plants were well nodulated and the nodules were large and pink in colour, indicating that they were effective. One point of interest, not related to nodulation, was that of a further 30 pots of treated plants left for observation, 15 were showing inflorescence formation some 50 days after treatment and only 2 out of 30 untreated were at a similar stage of development.

The effect of gibberellic acid on the growth of the nodule-forming organism was also tested using a turbidimetric method and growing the organism in wheat extract[3] and sauerkraut[4] media. The concentrations of gibberellic acid used were 1, 25, 50, 100 and 1,000 p.p.m. and readings were taken daily for 14 days. None of the concentrations used had any adverse effect on the growth of *Rhizobium trifolii* (strain 157).

Table 2

	No. of nodules per plant	Dry weight of nodules per plant (mgm.)
Plants sprayed with gibberellic acid	20	3
Plants sprayed with water	21	3

It would appear, then, that gibberellic acid, when used in the quantities indicated, has no adverse effect on the nodulation of white clover either in aseptic agar or in soil culture or on the growth of the nodule-forming organism.

Thanks are due to J. Anderson and C. McCombie for technical assistance and to Plant Protection, Ltd., which supplied the gibberellic acid for experimental purposes.

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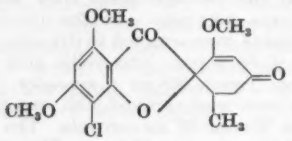
Some Cytological Effects of Griseofulvin

Griseofulvin is a fermentation product of three species of *Penicillium*—*P. patulum*, *P. griseofulvin*, and *P. janczewski*—which, in very low concentration, suppresses growth and induces striking changes in the hyphæ of a number of fungal species[1].



Griseofulvin

In laboratory mammals the lethal dose is high; Wistar rats of either sex tolerate a daily dose of 2 gm./kgm. given intraperitoneally in aqueous suspension for several days. When the tissues from rats dosed at this level for four days and killed on the fifth were examined histologically, we found the seminal epithelium to be severely damaged and in many places completely necrotic (Fig. 1). The intestinal epithelium also showed abnormalities, but these were less marked. The median lethal dose to rats by intravenous injection is of the order of 400 mgm./kgm. and we have found that some 6 hr. after a single intravenous dose of griseofulvin (100 or 200 mgm./kgm.) a striking arrest of mitosis in metaphase is evident in sites of mitotic activity in the rat. It is very marked in the bone marrow (Fig. 2*a*) and intestine (Fig. 2*b*) and, in rats bearing transplanted tumour (Walker carcinoma 256 or a lymphosarcoma), in the growing tumour tissue. Cells arrested in metaphase show, in varying degree, disorientation and scattering of the chromosomes through the cytoplasm (Fig. 3) such as is seen after colchicine, and in some instances beading or pyknosis of the chromosomes. Interference with mitosis in the bone marrow is reflected in a profound fall in the numbers of circulating red and white blood cells. In rats 24 hr. after this single dose the bone marrow is congested and contains little hæmopoietic tissue; mitotic figures are infrequent but mostly appear normal, while pyknotic and degenerate nuclei are still occasionally seen. In spite of these profound effects the rats appear little affected in general condition and at no

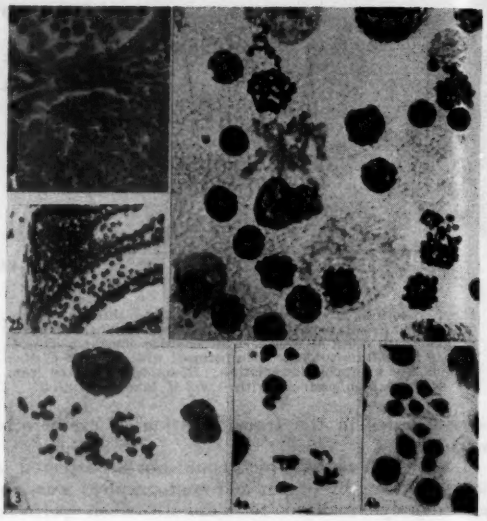


Fig. 1. Section of seminiferous tubules of a rat given griseofulvin intraperitoneally in aqueous suspension, 2 gm./kgm. daily for four consecutive days and killed on the fifth day. Hæmatoxylin and eosin. (×170)

Fig. 2. Tissues of a rat 6 hr. after a single intravenous dose of griseofulvin, 200 mgm./kgm., showing arrest of mitosis in metaphase. *a*, Bone marrow, squash preparation, Feulgen stain (× 600); *b*, intestinal crypts, section, Feulgen. (× 85)

Fig. 3. Bone marrow of a rat after a single intravenous dose of griseofulvin, 200 mgm./kgm., showing at 5 hr. scattering of metaphase chromosomes. Squash preparations, Feulgen stain. (× 600)

Fig. 4. Root-tips of *Vicia faba* after continuous exposure to supersaturated aqueous griseofulvin for *a*, 4 hr., and *b*, 16 hr. Feulgen stain, squash preparations. (× 200)

stage show very obvious signs of intoxication. Recovery in most of the affected tissues proceeds rapidly after 24 hr., although the effects of interference with spermatogenesis are still discernible in the testes at least 10 days after the single dose.

The true solubility of griseofulvin in water at room temperature is about 10 μgm./ml. Supersaturated solutions containing 20–40 μgm./ml. can be prepared by dissolving in water boiling under reflux (1 hr.), cooling and filtering. Growing roots of *Vicia faba* were immersed in such solutions for varying periods and their tips, fixed either immediately or after varying periods of recovery in tap water, were studied cytologically. Supersaturated solutions of griseofulvin produce some delay in mitosis at metaphase in bean roots within ½–1 hr. of their immersion, but a more striking feature of its action is the induction of multipolar mitosis. In many cells, after separation of the chromatids, the total complement of chromosomes segregates into irregular groups, up to five in number, which are then reconstructed as nuclei of varying size within the original cell (Fig. 4*a*). Cell-cleavage follows in some instances resulting in small mononuclear cells of variable size (Fig. 4*b*). In 'recovery' experiments in which the root-tips were finally exposed to colchicine (0·05 per cent aqueous for 4 hr.) before fixation a small number of tetraploid cells was seen, but under the conditions of our experiments the agent gives rise to fewer polyploid nuclei than would be expected with colchicine itself.

The effects of griseofulvin upon mitosis in some respects resemble those of colchicine; but in rats, at least, it seems much less generally toxic in doses required to produce equivalent metaphase arrest.

These preliminary observations are published in the belief that this agent may prove useful to workers in the field of cytology and genetics.

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Gibberellic Acid and the Physiological Genetics of Flowering in Peas

In peas (*Pisum sativum*) Barber[1] has shown that the *Sn* gene which is dominant for a delay in flowering to a higher node has at least four other pleiotropic effects. The gene induces competence to respond to photoperiod and vernalization; it delays the formation of the first leaf with more than two leaflets; and it causes a small reduction in internode length. The reduction in length is only about 10 per cent of that caused by segregation at the *Le* locus. These effects were investigated by appropriate crosses among the four commercial varieties: Telephone (late flowering, tall: *Sn Le*), Greenfeast (late, dwarf: *Sn le*), Alaska (early, tall: *sn Le*) and Massey (early, dwarf: *sn le*). The crosses have also given some evidence that segregation at the *Le* locus may modify the action of *Sn*, *Le Sn* plants flowering about 0·5 node later than *le Sn* plants in appropriate F_2s. The modifying effect of *Le* is 5–10 per cent of the effect of *Sn*. Segregation at the *Le* locus appears to have no effect on an *sn* background.

Brian and Hemming[2] have shown that segregation at the *Le* locus affects some aspect of the metabolism of the gibberellins. In view of the over-lapping pleiotropic effects of segregation at the *Le* and *Sn* loci, we have made an investigation of the effect of gibberellic acid on flowering in the four varieties. The varieties were combined factorially with two photoperiods (18 hr. and 9 hr.), two vernalization treatments (unvernalized and three weeks at 4° C.), and two gibberellic acid treatments (none and 1 μgm. applied to dry seed prior to germination).

The results for node of first initiated flower are given in Fig. 1. The reaction of the varieties to photoperiod and vernalization is as described by Barber[1], late (*Sn*) varieties flowering at a lower node in long days and when vernalized, while early varieties (*sn*) show no response to either environmental variable. The effect of gibberellic acid is to delay initiation of flowering in all varieties. The mean delay varies from about 0·5 node in Alaska to 1·7 node in Massey, giving a delay in time of about one to three days. Gibberellic acid usually causes considerable abortion of flower rudiments so that the delay in production of open flowers is variable and may be considerably longer than three days.

There is a statistically significant interaction between *Le* and gibberellic acid, the effect of the acid on flowering being less in the tall varieties. Brian[3] has shown similarly that the effect of gibberellic acid in controlling growth in length of stem is less in tall than in dwarf varieties. There are no highly significant gibberellic acid × *Sn* interactions. There is an apparently highly significant gibberellic acid × V interaction in long days. However, this interaction seems largely to be due to the behaviour of Massey,

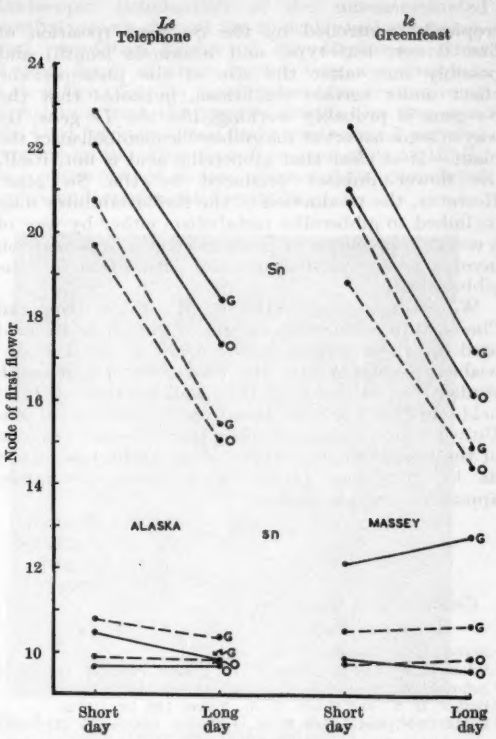

Fig. 1. Effects of gibberellic acid on node of initiation of flowers in four varieties of peas under different photoperiods (short-day, 9 hr.; long-day, 18 hr.) and vernalization treatments (unvernalized; vernalized by 3 weeks at 4° C.). ●– –●, Vernalized; ●——●, unvernalized; *G*, treated with gibberellic acid; ○, untreated

which has proved to be anomalous in this experiment. Further experiments to test in detail the behaviour of Massey to gibberellic acid have given no indication of any effect of vernalization and photoperiod on the delay in flowering induced by the gibberellic acid. These latter experiments included both higher total dose and doses applied after germination to plumule and leaves.

There is some evidence that in *Sn* plants gibberellic acid treatment followed by vernalization may increase the effect of photoperiod. This is in curious contrast to the behaviour of plants not treated with gibberellic acid, where Barber[1] has shown that prior vernalization reduces the photoperiodic response. However, for unknown reasons this competitive effect of vernalization on photoperiod is much weaker in the untreated plants in our experiments. Further experiments are planned to test the significance of these complex interactions.

In addition to the effect on flower-initiation, these experiments have shown that gibberellic acid, like the *Sn* gene, delays the production of leaves with more than two leaflets.

Barber and Paton[4,5] have suggested that the *Sn* gene in peas exerts its effect by producing a hormonal substance which delays the initiation of flowers. Barber[1] concluded that the production of the inhibitor is responsible for the competence of late varieties to respond to photoperiod and vernalization, the inhibitor being selectively destroyed during long days and at low temperatures. The fact that gibberellic acid certainly affects three of those characteristics pleio-

tropically controlled by the *Sn* gene (position of first flower, leaf type, and internode length) and possibly may alter the size of the photoperiodic effect under certain conditions, indicates that the *Sn* gene is probably working, like the *Le* gene, by way of some aspect of the gibberellic metabolism of the plant. It is clear that gibberellic acid is not, itself, the flower-inhibitor produced by the *Sn* gene. However, the production of the flower-inhibitor may be linked to gibberellin metabolism either by way of a common precursor or more indirectly by a reaction involving the production and utilization of the gibberellins.

We wish to thank Dr. P. W. Brian (Imperial Chemical Industries) for the gift of the gibberellic acid used in these experiments. One of us (I. C. M.) wishes to acknowledge the assistance of a research studentship of the C.S.I.R.O. and another (J. I. S.) held the I.C.I.A.N.Z. Research Fellowship of the University of Tasmania. The Rural Credits Division of the Commonwealth Bank of Australia has helped us by providing funds for technical assistance, apparatus and glasshouses.

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Effect of Trauma on Wool Growth

A recent communication[1] indicated that mechanical trauma such as cutting or scratching the rabbit skin was sufficient to cause a sudden stimulation of hair growth around the site of injury. This effect was observed most dramatically in the quiescent phase of the hair growth-cycle. Because hair replacement in the mouse, rat, and rabbit is discontinuous and occurs in cyclical waves of active growth, Ghadially[1] suggested that the mechanical damage caused quiescent skin to become active and as a result stimulated hair growth. In the case of guinea pigs and man, he reported no gross hair growth-cycle but each hair showed an independent cycle of growth and quiescence. However, he did not indicate whether the hair types from the latter groups would exhibit stimulated growth from trauma.

In our studies on the growth of wool as related to intake of protein, wool samples were collected monthly from tattooed areas on the right shoulder. During the course of sampling we have observed that simple mechanical trauma, as judged by 'bumps' or elevations on the skin, has resulted in a stimulation of growth of wool on the elevated areas. These elevations resulted from the sheep being bumped on the shoulder area as it entered an individual feeding pen. This phenomenon was not noted during subsequent sampling periods and consequently was considered to be of a temporary nature. Wool samples were collected from the elevated area (Sample 1) and from the surrounding area (Sample 2) and 50 fibres were measured for length and thickness. The results are shown in Table 1.

Table 1

	Sample 1	Sample 2
Crimped length (mm.)	14·0	12·5
Decrimped length (mm.)	18·4 (±1·5)*	17·7 (± 1·9)*
Ratio : decrimped length/ crimped length	1·3	1·4
Fibre thickness (μ)	20·4 (± 3·5)*	17·7 (± 2·4)*

* Standard deviation

It is evident from these determinations that there was an increase in the average lengths ($P < 0.05$) and thickness ($P < 0.01$) of those fibres exposed to trauma when compared with those from the surrounding area. Ghadially[1] has indicated that mechanical damage caused quiescent skin to become active and as a result stimulated hair growth. In the case of sheep it was evident that growth of wool was stimulated although the fibre is a continuously growing filament and not subject to periods of quiescence[2]. Haddow *et al.*[3] and Haddow and Rudall[4] showed that there was a greater density of blood vessels in the skin of rats at the advancing edge of the zone of active hair growth. Durward and Rudall[5] also found that the blood vessel network around the follicle was most dense when the hairs were actively growing, but became reduced during the resting stage of the hair growth-cycle. Ferguson *et al.*[6] deduced that in sheep higher temperatures influenced growth of wool by causing vasodilation and a consequent increased flow of nutrients to the follicle. Ferguson[7] also showed that vasodilation caused by unilateral sympathectomy increased growth of wool on the side of the body in which the nerves had been cut. In view of this it is suggested that trauma, with its concomitant increase in blood supply to the site of injury, stimulated growth of wool.

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Isolation and Pure Culture of *Monoblepharis*

Although the genus *Monoblepharis* has been known since 1871 and its species have been collected in many parts of the world[1], there has been no account of its isolation and growth in pure culture, so in 1957 pure culture studies were begun. The investigation is not yet complete, but one of the techniques developed is reported here in view of its possible interest to other mycologists.

The inoculum was derived from natural growths of *Monoblepharis* sp. on twigs of *Quercus robur* L.[1]. Hyphal tufts were teased out under a wide-field binocular microscope, and washed by transference to at least ten successive dishes of sterile distilled water. A small portion of one of these hyphal tufts was then transferred to a cavity slide containing a drop of sterile distilled water and the material observed at a higher magnification (× 500). Tips of hyphæ from a mycelium bearing sexual reproductive organs (by means of which species are identi-

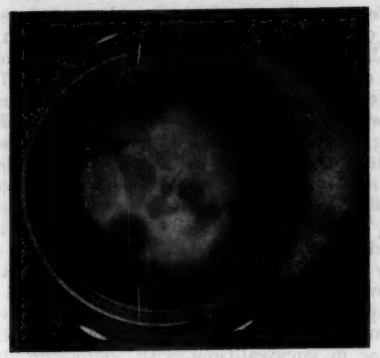

Fig. 1. Initial isolate of *M. sphaerica* after 10 days at 15° C. Photographed from lower surface

fied), were severed with sterile cutting needles and transferred by Pasteur pipettes to Petri dishes of agar.

The agar used for initial inoculations was poured in a thin layer, not more than 2–3 mm. thick, in 9-cm. Petri dishes and allowed to dry for a day or so until all surface moisture had disappeared. A 1 per cent tryptone medium solidified with 1 per cent agar, and having a final *p*H of 6·8 was used.

Limitation of the spread of bacterial contaminants over the surface of the agar was effected by Raper's[2] device. This consists of a van Tieghem ring to one end of which are fixed three glass beads $\frac{1}{3}$–$\frac{1}{2}$ mm. in diameter (Fig. 1). One of these rings was placed in the centre of each Petri dish, with the glass beads resting on the base. Enough agar was added to bring its surface not more than half-way up the side of the ring. The inoculum was transferred to the area within the ring together with a few drops of sterile distilled water, care being taken to see that water did not reach the top of the ring.

After 10 days incubation at 15° C., bacterial colonies and mycelial growth were seen within the ring, with some of the hyphæ extending down into the agar, growing under the ring and into the medium lying beyond it. The contaminating bacteria were retained at the surface of the agar within the ring (Fig. 1).

Fig. 2. Portion of mycelium after 12 days at 15° C., showing sporangial formation. (Agar squash, unstained; × *c.* 270)

Microscopic examination of the uncontaminated mycelial growth showed the typical, regularly vacuolated, vegetative hyphæ of *Monoblepharis*. After 12 days many of these hyphæ bore a sporangium at their tips (Fig. 2). Small cubes of agar containing hyphal tips from the growth outside the ring were then used for inoculating flasks containing 1 per cent tryptone broth. After four days incubation at 15° C., the colonies formed showed characteristic, vacuolated hyphæ and sporangial formation.

Fig. 3. Single spore colonies, 7 days after inoculation with zoospore suspension from liquid culture

The successful growth of *Monoblepharis* in liquid culture made the following technique for obtaining single spore isolations possible. The needle of a sterile hypodermic syringe was inserted through the cotton-wool plug into a 4-day-old culture. Several ml. of the liquid in the flask were withdrawn and a sample examined for the presence of zoospores. These being present, Petri dishes containing suitable media were each inoculated with a few drops of suspension from the syringe, which were spread over the surface of the medium. Fig. 3 shows such a culture after seven days incubation at 20° C. Re-inoculations were easily made from the single spore colonies thus formed. *M. sphaerica* Cornu, *M. insignis* var. *minor* Perrott and *M. macrandra* (Lagerheim) Woronin, have been isolated in this way.

Raper's device for limiting the spread of bacterial contaminants contributed to the success of these isolations; but modification of the technique to include the use of the ring as a temporary reservoir for a small amount of sterile water also seemed to be an important factor in the initial growth of *Monoblepharis* sp. on a solid medium. This was demonstrated when isolations were made on 1 per cent tryptone agar to which was added a 1 : 30,000 dilution of rose bengal together with 3 μgm. of streptomycin per ml. of medium[3]. Although the antibiotic and rose bengal successfully inhibited the growth of bacterial contaminants, a significantly larger number of successful growths of *Monoblepharis* sp. were obtained from those cultures where 'Raper's rings' had been used compared with those in which the rings were omitted.

Fuller reports of these and related investigations will appear elsewhere.

Thanks are due to Prof. C. W. Wardlaw of the University of Manchester and Prof. A. R. Gemmell of the University College of North Staffordshire for their interest in this work, and to the Royal Society for a research grant.

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Aldosterone and Experimental Hepatic Necrosis

There is some evidence that aldosterone, besides its potent effects on electrolyte metabolism, also possesses some cortisone-like activity. The data available, however, are rather scanty and somewhat contradictory. In recent years an effect of cortisone and of related hormones has been described which appears to be characteristic for the 'glucocorticoid' group of adrenocortical steroids. If given in a daily dose of 1 mgm. per 100 gm. body-weight, cortisone doubles or trebles the survival-time of rats fed a diet containing yeast as the only source of protein without, however, significantly altering the incidence of fatal liver necrosis caused by this deficient diet[1,2]. Characteristically, this effect of cortisone still occurs if the administration of this hormone is started as late as the last third of the experimental period[3]. Of the hormones examined so far only cortisone, cortisol and adrenocorticotrophic hormone have significantly prolonged the survival time; progesterone, œstrogen, testosterone, œstrogen plus testosterone, and deoxycortone acetate have been without effect (Aterman, K., unpublished work). Corticosterone is now being investigated. In view of the lack of data on the biological actions of aldosterone it was considered of interest to see how its activity would compare with that of cortisone and of deoxycortone acetate in affecting the course of experimental hepatic necrosis.

14 pairs of male rats bred in the Department of Anatomy, Birmingham, weighing 31–41 gm., were weaned on the twenty-first day of life, the first day of the experiment, and were given the 'necrogenic yeast diet' of Lindan and Himsworth[4]. On the eighteenth day of the experiment the administration of D-L-aldosterone-21-monoacetate (Ciba) to one brother of each pair was started. It is apparent from Table 1 that the daily dose of 10 μgm. of aldosterone had no effect on the survival-time, but a dose of 50 μgm. daily prolonged the survival-time in every animal, the effect being somewhat more pronounced if the dose of aldosterone was increased to 75 μgm. Of interest also is that the treated rat of group 14 died within 30 hr. of the last dose of aldosterone having been given when all the aldosterone available had been used up. The cause of death in every case was necrosis of the liver. Statistical analysis of the differences obtained shows a probability value of less than 0·02, if all the animals treated with aldosterone are considered, and a probability value of less than 0·01, if the four rats given the lowest dose of aldosterone are excluded on the assumption that the amount of aldosterone given was too small. This assumption appears justified if the increase in survival-time with increasing doses of aldosterone, which was statistically just significant ($P<0·05$), is taken into consideration. These results, therefore, suggest that in the system examined here aldosterone has some 'glucocorticoid' activity and differs significantly from deoxycortone acetate which in doses of 0·5 and 2·5 mgm. daily has been completely ineffective. A more extensive study of this effect will, however, have to be undertaken when more aldosterone becomes available.

Table 1. The Effect of Aldosterone on the Survival-Time (in days) of Littermate Rats fed on the 'Necrogenic Yeast Diet'

Pair No.	Control	Aldosterone		Difference in survival-time
	Days	Dose	Days	
1	32	10 μgm.	41	+ 9
2	31		26	− 5
3	32		26	− 6
4	30		36	+ 6
5	23	50 μgm.	31	+ 8
6	23		24	+ 1
7	23		30	+ 7
8	26		31	+ 5
9	22		25	+ 3
10	28		29	+ 1
11	26		32	+ 6
12	22	75 μgm.	40	+ 18
13	31		33	+ 2
14	28		42	+ 14

I wish to thank Prof. R. Meier of Ciba, Ltd., Basle, for the gift of aldosterone, and Miss H. Sorrill for her technical assistance.

K. Aterman

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Aug. 29.

[1] Schwarz, K., *Science*, **113**, 485 (1951).
[2] Aterman, K., *Endocrinol.*, **60**, 711 (1957).
[3] Aterman, K., Meeting of Federation of American Societies for Experimental Biology, Chicago, Illinois (1957).
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Atypical Segregation of Haptoglobin Types in Man

Smithies and Ford-Walker[1] have suggested that the three haptoglobin phenotypes, namely, 1–1, 2–1, and 2–2, detected by starch gel electrophoresis are determined by a pair of allelic genes Hp^1 and Hp^2. The findings in the eighteen families reported by Smithies and Ford-Walker and also in 106 families reported later by Galatius-Jensen[2] were fully consistent with this hypothesis. Furthermore, the frequencies of the phenotypes in different populations agree well with those expected assuming a Hardy-Weinberg equilibrium[3–4].

We have recently investigated a further 107 families, and while our results for the most part support this simple genetical hypothesis a small number of exceptions to the expected pattern of segregation were encountered.

The electrophoresis was carried out on plasmas to which sufficient hæmoglobin to saturate the haptoglobins had been added. The discontinuous buffer system described by Poulik[5] was used. The haptoglobin–hæmoglobin complexes were afterwards detected with a benzidine reagent. This technique reveals an even more complicated pattern of haptoglobin components than has previously been reported[2,6], but no ambiguity in classification was encountered. The kind of patterns which were obtained are shown diagrammatically in Fig. 1. While only a single *HbHp* complex can be detected

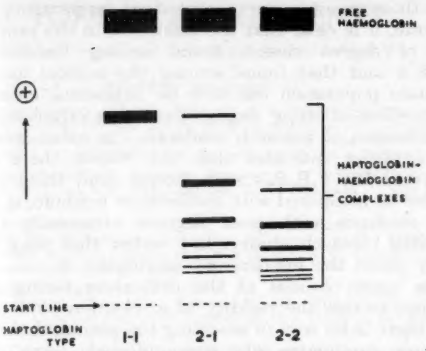

Fig. 1. Diagram showing the pattern of haptoglobin–hæmoglobin complexes after electrophoresis in starch gel using a discontinuous buffer system (ref. 5), the complexes being detected with a benzidine reagent

in type 1–1 plasmas, as many as seven such components can often be seen in types 2–1 and 2–2. Each of the components in the 2–1 plasmas has a mobility different from any of those in the 2–2 plasmas. A minor component, however, is regularly present in the 2–1 plasmas which has the same mobility as the single component in the 1–1 plasmas. Excess free hæmoglobin moves well ahead of the fastest *HbHp* complex.

Table 1 shows the results of the different types of matings. In only three out of 472 individuals in these families could no haptoglobins be detected and there was no evidence of recent hæmolysis to account for these cases[7,8]. There were nine out of 258 whose haptoglobin type was incompatible with those of their parents on the genetical hypothesis (Table 1). Four of these exceptions can probably be attributed to illegitimacy and in three of them this conclusion is supported by blood-group studies. The remaining five unusual segregants all occurred in three closely related families, kindred *B* (Fig. 2). Four of the exceptional offspring were incompatible with their mothers' haptoglobin types so that illegitimacy could be excluded. One of the three individuals in the series with no detectable haptoglobins also occurred in one of these families.

The findings in kindred *B* suggest that some unusual allele or modifying gene may occur. One possibility is that there exists a rare allele Hp^0 such that Hp^1Hp^0 individuals are phenotypically 1–1 and Hp^2Hp^0 individuals are phenotypically 2–2. The pedigree could then be explained if individuals I 2, 3 and 5 were Hp^1Hp^0 and individuals II 2, 5, 6, 10 and 11 were Hp^2Hp^0. The individual with no detectable haptoglobins, II 7, might conceivably be a homozygote Hp^0Hp^0, but this requires that the unrelated

Table 1. SEGREGATION OF HAPTOGLOBIN TYPES IN 107 FAMILIES. EXCEPTIONAL SEGREGANTS ARE MARKED WITH AN ASTERICK

Mating Father × Mother	No. of matings	Offspring: Haptoglobin types 1–1	2–1	2–2	Total
1–1 × 1–1	4	11	—	—	11
1–1 × 2–1	5	7	8	1*	16
2–1 × 1–1	3	3	5	—	8
1–1 × 2–2	7	—	22	—	22
2–2 × 1–1	6	2*	11	4*	17
2–1 × 2–1	23	18	23	11	52
2–1 × 2–2	26	—	33	19	52
2–2 × 2–1	19	—	25	21	46
2–2 × 2–2	14	—	2*	32	34
Totals	107	41	129	88	258

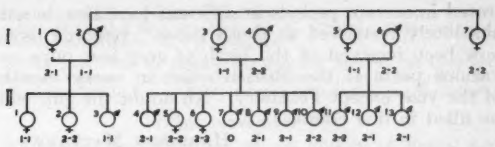

Fig 2. Pedigree of kindred *B* showing atypical segregation: 1–1, 2–1 and 2–2 refer to the haptoglobin types of Smithies (ref. 1); 0 signifies that no haptoglobins were detected

father I 4 should carry the Hp^0 gene, which is presumably rather rare. Alternatively, II 7 might represent an Hp^2Hp^0 individual whose level of haptoglobin was below the limit of detection. The fact that two of his 2–2 sibs and a 2–2 aunt, I 7, had rather weakly developed haptoglobins is perhaps rather in favour of this explanation. On the other hand, one might postulate the presence in homozygous form of a modifying, non-allelic gene in the phenotypically 1–1 individuals in the parental generation such that in an Hp^1Hp^2 individual the phenotype was indistinguishable from Hp^1Hp^1. In this case the observed segregation would be possible but the individual with no haptoglobins would be left unexplained. Other hypotheses can also be constructed and no doubt the point will only be clarified when further unusual families of this sort are identified.

While we do not feel that the atypical segregation in this kindred upsets the general validity of the genetical hypothesis of Smithies and Ford-Walker, with which most of our results are in agreement, the existence of such an exception is of obvious significance if, as has been suggested[1,2], haptoglobin typing is contemplated for medico-legal purposes.

Full details of this work will be published elsewhere.

We would like to acknowledge the help of Profs. E. Silvestroni, I. Bianco and B. Latte in the collection of some of the material.

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July 30.

[1] Smithies, O., and Ford-Walker, N., *Nature*, **176**, 1265 (1955); **178**, 694 (1956).
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Calving Time of Grey Seals

THE interesting account of the Glasgow University Expedition to North Rona and Sula Sgeir in *Nature* of September 20, p. 775, records that a grey seal calved successfully on North Rona as early as July 6, and adds: "the earliest calves recorded hitherto for Great Britain have been born in mid-August". Research during the past few years has shown that the time for calving of the grey seal, although concen-

trated in certain periods in different localities, is not absolutely restricted to those times. Records have now been received of the birth of grey seal pups on various parts of the British coast in every month of the year except February. No doubt the gap will be filled in due course.

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Undergraduate Academic Record of Fellows of the Royal Society

In a previous communication[1] concerning the problem of the selection of students for scientific research, the use of F.R.S.'s as a criterion group of research ability was described, and the proportion of degree classes gained within this group was reported. Such results could give no precise idea of the relation between degree class and research ability unless compared with the results gained by the research population from which the F.R.S.'s emerged. The data necessary for such a comparison have now been collected, and are given in Tables 1 and 2. Only one part of the F.R.S. population has been used for the purpose of this comparison, namely, those who graduated from Cambridge during the period 1920–39. In gathering a representative sample of the research population at Cambridge during the same period, each F.R.S. was matched as closely as possible with a research student of the same sex, who read the same subject, who graduated in the same year, and who has not yet become a Fellow of the Royal Society. Apart from these requirements the sampling for the non-F.R.S. group was random. The Tripos results for both groups are set out side by side in Table 1, the figures in brackets representing the totals on which the percentages are based. Table 2 shows the results for both groups in the last Tripos examination taken, classified in terms of the faculty to which each individual belonged.

Table 1. Cambridge Tripos Results for Part 1 and Part 2

Class		Cambridge 1920–39	
Part 1	Part 2	F.R.S.	Non-F.R.S.
1	1	(50) 54·9%	(60) 65·9%
2 or 3	1	(8) 8·8%	(6) 6·6%
1	2 or 3	(10) 11·0%	(8) 8·8%
2 or 3	2 or 3	(7) 7·7%	(8) 8·8%
1		(12) 13·2%	(6) 6·6%
2 or 3		(4) 4·4%	(3) 3·3%

It will be seen that the proportion of degree classes for the two groups are remarkably similar, both before and after they are broken down into faculties. Owing both to the size of the groups and the degree of similarity between them, it is statistically most unlikely that a significant difference in the proportions is disguised in this case by inadequate sampling.

If these results are accepted as approximately accurate, it is clear that the difference in the proportion of degree classes found among Cambridge F.R.S.'s and that found among the normal undergraduate population can now be explained entirely as an effect of using degree class as a criterion for the selection of research students. In other words, this evidence indicates that the reason there are relatively few F.R.S.'s with second- and third-class degrees as compared with students as a whole, is not that students with poor degrees necessarily lack potential research ability, but rather that they are rarely given the opportunity to display it.

The most obvious of the difficulties facing any attempt to test the validity of a selection method is that there is no way of assessing the potential ability of those candidates who were rejected. Any conclusions about such potential abilities must therefore take the form of an inference, dependent on evidence internal to the group which the method accepts. Despite this limitation, two inferences do seem at least provisionally to be justified by the present evidence. They are as follows.

(1) During the period 1920–39, a scientific research student at Cambridge with a second-class degree had the same chance of becoming a Fellow of the Royal Society as had a research student with a first-class degree. Or, more generally, once selected for research, by whatever criteria, a Cambridge student's degree class was irrelevant to his research ability.

(2) During the period 1920–39, the class of a Cambridge student's degree was irrelevant to his potential research ability, whether he happened to be selected for research or not.

Against the second inference it might be argued that in spite of the two F.R.S.'s with third-class degrees, the evidence does not exclude the possibility of a sizeable correlation between degree class and research ability among students with unusually poor degrees. Although degree class is predictively useless in dealing with candidates for research with firsts and seconds, it might nevertheless still have a limited predictive use in dealing with candidates with thirds.

Table 2. Results and Faculties of Last Tripos Taken

Class	Cambridge 1920–39					
	F.R.S.			Non-F.R.S.		
	Nat. Sci.	Maths.	Mech. Sci.	Nat. Sci.	Maths.	Mech. Sci.
1	(44) 48·3%	(19) 20·9%	(7) 7·7%	(45) 49·4%	(21) 23·1%	(6) 6·6%
2	(15) 16·5%	(3) 3·3%	(1) 1·1%	(15) 16·5%	(1) 1·1%	(3) 3·3%
3	(1) 1·1%	(—) —	(1) 1·1%	(—) —	( ) —	(—) —

Unavoidably the validity of such inferences as these varies in inverse proportion to their relevance to the original problem; and although, considered separately, this and other more tenuous objections may appear somewhat slight, their accumulative effect on the second inference could well be considerable. However, in view of the clear-cut nature of the present evidence, it would be surprising if even the less justified of these inferences proves eventually to be substantially untrue.

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Oct. 10.

[1] Gross, C., and Hudson, L., *Nature*, **182**, 787 (1958).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, November 10

BRITISH SOCIETY FOR THE HISTORY OF SCIENCE, PHILOSOPHY OF SCIENCE GROUP (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. R. B. Braithwaite: "Identifications as the only Axioms for a Science".

ROYAL INSTITUTION, LIBRARY CIRCLE (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Captain J. L. Pritchard: "The First Centuries of Flight".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (joint meeting with the Woolwich Polytechnic Scientific Society, at the Woolwich Polytechnic, London, S.E.18), at 7.30 p.m.—Dr. A. G. Davies: "The Stereochemistry of Some Reaction Mechanisms".

BRITISH PSYCHOLOGICAL SOCIETY (at Birkbeck College, Malet Street, London, W.C.1), at 8 p.m.—Dr. H. Himmelweit: "The Relevance to Social and Child Psychology of a Study of the Effects of Television on Children".

ROYAL GEOGRAPHICAL SOCIETY (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Dr. Paul A. Siple: "South Pole Station".

Tuesday, November 11

UNIVERSITY OF LONDON (at Queen Mary College, Mile End Road, London, E.1), at 1.30 p.m.—Mr. Ritchie Calder: "H. G. Wells".*

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Prof. H. S. W. Massey, F.R.S.: "Exploration of Space".*

ZOOLOGICAL SOCIETY OF LONDON (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

INSTITUTION OF THE RUBBER INDUSTRY, LONDON SECTION (at the Royal Society of Tropical Medicine and Hygiene, Manson House, 26 Portland Place, London, W.1), at 5.30 p.m.—Mr. C. H. Gregory: "Rubber Products for the Motor Industry". 7 p.m.—Mr. S. G. Fogg: "Natural Rubber Compounds for High Temperature Service".

UNIVERSITY OF LONDON (at the Imperial College of Science and Technology, London, S.W.7), at 5.30 p.m.—Prof. S. R. Sparkes: "Engineering Structures—Teaching and Research" (Inaugural Lecture).

INSTITUTION OF MECHANICAL ENGINEERS, AUTOMOBILE DIVISION (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. T. C. F. Stott: "Fatigue Testing of Vehicle Components".

SOCIETY OF CHEMICAL INDUSTRY, CHEMICAL ENGINEERING GROUP (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. W. B. Wright and Mr. W. Elland: "The Integrated Iron and Steel Works".

ROYAL AERONAUTICAL SOCIETY (in the Theatre, Park Lane House, 45 Park Lane, London, W.1), at 7 p.m.—Dr. J. Williams: "Boundary Layer Control to Produce High Lift at Low Speeds".

ROYAL AERONAUTICAL SOCIETY, GRADUATES' AND STUDENTS' SECTION (at 4 Hamilton Place, London, W.1), at 7.30 p.m.—Sir Gerard D'Erlanger: "The Air Transport Auxiliary".

Wednesday, November 12

GEOLOGICAL SOCIETY OF LONDON (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. W. S. McKerrow and Dr. C. J. Campbell: "The Lower Palæozoic Rocks of North-West Galway"; Dr. J. F. Evernden (University of California): "Potassium/Argon Dating of Tertiary and Pleistocene Rocks".

SOCIETY OF INSTRUMENT TECHNOLOGY, CONTROL SECTION (at Manson House, Portland Place, London, W.1), at 6 p.m.—Dr. P. Fellgett: "Some Applications of Control Technique in Astronomy".

SOCIETY OF CHEMICAL INDUSTRY, CORROSION GROUP (joint meeting with the PLASTICS AND POLYMER GROUP, at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. H. G. Cole and Mrs. V. E. Rance: "Plastics and other Polymers as Sources of Corrosive Vapours"; Mr. A. C. Docherty and Mr. H. Hughes: "Plastics for Protection Against Corrosion".

Wednesday, November 12—Thursday, November 13

ROYAL SOCIETY (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 2.30 p.m. on Wednesday and 10 a.m. on Thursday—Discussion on "Space Research" opened by Prof. H. S. W. Massey, F.R.S.

Thursday, November 13

UNIVERSITY OF LONDON (in the Anatomy Theatre, University College, Gower Street, London, W.C.1), at 1.15 p.m.—Dr. A. Maccoll: "Some Impressions of the Colleges in West Africa and the West Indies".*

PHYSICAL SOCIETY, LOW TEMPERATURE GROUP (at the Royal School of Mines, London, S.W.7), at 4 p.m.—Dr. J. M. Lock: "Cryotrons".

ROYAL STATISTICAL SOCIETY (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5 p.m.—Mr. C. B. Winsten: "Geometric Distributions in the Theory of Queues".

INSTITUTION OF MECHANICAL ENGINEERS, HYDRAULICS GROUP (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Flow—the Origin and Nature of Turbulence: Boundary-Layer Occurrences".

CHEMICAL SOCIETY (at the Royal Institution, 21 Albemarle Street, London, W.1), at 7.30 p.m.—Prof. Dr. K. Clusius: "Chemical and Technological Aspects of ^{15}N-Chemistry".

ROYAL INSTITUTE OF CHEMISTRY, LONDON SECTION (at Croydon Technical College, Fairfield, Croydon, Surrey), at 7.30 p.m.—Dr. G. B. Cook: "The Use of Radioisotopes in Industry and Medicine".

Friday, November 14

BIOCHEMICAL SOCIETY (at the National Institute of Medical Research, The Ridgeway, Mill Hill, London, N.W.7), at 2 p.m.—377th Meeting.

INSTITUTION OF MECHANICAL ENGINEERS (in conjunction with the STEAM GROUP, at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Dr. T. Furman and Mr. H. Hampson: "Experimental Investigation into the Effects of Cross Flow with Condensation of Steam and Steam–Gas Mixtures on a Vertical Tube".

ROYAL INSTITUTION (at 21 Albemarle Street, London, W.1), at 9 p.m.—Mr. G. G. Gouriet: "Colour Television—Progress During the Last Decade".

Friday, November 14—Saturday, November 15

BRITISH SOCIETY FOR IMMUNOLOGY (joint meeting with the BRITISH ASSOCIATION OF ALLERGISTS, at the Wellcome Building, Euston Road, London, N.W.1), at 2.30 p.m. Friday—Symposium on "Immunological Aspects of Allergic Disorders". Chairman: Dr. D. Blair Macaulay.

Saturday, November 15

BRITISH PSYCHOLOGICAL SOCIETY, EDUCATION SECTION (in conjunction with the ASSOCIATION FOR TEACHERS IN COLLEGES AND DEPARTMENTS OF EDUCATION, in the Assembly Hall, University of London Institute of Education, Malet Street, London, W.C.1), at 10 a.m.—Symposium on "Psychology in the Three-year Teacher-Training Course".

LONDON COUNTY COUNCIL (at the Horniman Museum, London Road, Forest Hill, London, S.E.23), at 3.30 p.m.—Mr. R. Bassindale: "The Natural History of Ghana".*

APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned:

JUNIOR LECTURER or LECTURER, and a LECTURER or SENIOR LECTURER IN THE DEPARTMENT OF BACTERIOLOGY—The Dean, Guy's Hospital Medical School, London, S.E.1 (November 14).

RESEARCH ASSISTANT, for work in the general field of photoconductance, absorption spectra and other electronic properties of ionic solids—Dr. F. C. Tomkins, Chemistry Department, Imperial College of Science and Technology, London, S.W.7 (November 15).

ASSISTANT LECTURER (with special qualifications in stratigraphy and/or palæontology) IN GEOLOGY—The Secretary, The University, Belfast (November 20).

ASSISTANT LECTURER (with special qualifications in applied mathematics) IN MATHEMATICS—The Registrar, The University, Manchester (November 22).

CARTOGRAPHIC DRAUGHTSMAN (able to compile and prepare maps for publication, and preferably geography graduate) IN THE DEPARTMENT OF GEOGRAPHY—The Registrar, The University, Leeds 2 (November 24).

TEMPORARY LECTURER IN MEDICAL AND VETERINARY ENTOMOLOGY—The Secretary, The University, Edinburgh (November 29).

RESEARCH FELLOW IN PÆDIATRIC PHYSIOLOGY IN THE DEPARTMENT OF PHYSIOLOGY, for the study of problems relating to the physiology of infancy and childhood—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (November 30).

SENIOR LECTURER IN ANATOMY (GROSS ANATOMY) at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, November 30).

SENIOR LECTURER IN BOTANY, and a LECTURER IN BOTANY—The Registrar, University of New England, Armidale, N.S.W., Australia, or The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (November 30).

LECTURER IN PHILOSOPHY at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 8).

LECTURER (competent to lecture in economic geology and structural geology) IN GEOLOGY at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 15).

LECTURER (with an honours degree in mathematics) IN MATHEMATICS WITHIN THE DEPARTMENT OF EXTERNAL STUDIES, University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 15).

RALSTON PROFESSOR OF ZOOLOGY in the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 15).

READER IN AERONAUTICS at Imperial College—The Academic Registrar, University of London, Senate House, London, W.C.1 (December 15).

RESEARCH FELLOW (with a good knowledge of electronics) IN THE DEPARTMENT OF PHYSICS, University of New England, Armidale, N.S.W., Australia, to engage in a research programme on spark discharges in association with Prof. J. M. Somerville—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, December 18).

PROFESSOR OF FORESTRY—The Registrar, University Registry, Oxford (December 24).

CHAIR OF BOTANY—The Registrar, The University, Hull (December 31).

CHAIR OF PHILOSOPHY in the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, December 31).

READER OR SENIOR LECTURER IN CLINICAL PHYSIOLOGY at Makerere College (University College of East Africa)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (January 1).

FISHERIES OFFICER (with a university degree in marine biology and suitable postgraduate experience) IN THE DEPARTMENT OF AGRICULTURE, Bahamas, to advise on fisheries conservation, introduce new fishing methods, and enforce the fisheries laws—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/27/04.

PLANT PATHOLOGIST/VIROLOGIST (with a good honours degree in a biological science and postgraduate training or experience in plant virus work) at the West African Cocoa Research Institute, Sub-station Ibadan, Nigeria, to carry out research on plant pathological problems relating to cocoa—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD/197/200/017.

RESEARCH ASSISTANT (chemistry graduate), to study anionic polymerization with emphasis on reaction mechanisms of stereospecific systems—The Head, National College of Rubber Technology, Northern Polytechnic, Holloway, London, N.7.

RESEARCH ASSISTANT (male or female) IN BIOCHEMISTRY—The Medical Superintendent, Western General Hospital, Edinburgh 4.

RESEARCH TECHNICIAN, to work on biochemical problems in a diabetic clinic and laboratory—The Personnel Officer, St. Thomas's Hospital, London, S.E.1.

SENIOR and JUNIOR PHYSICIST IN THE PHYSICS DEPARTMENT—The Clerk to the Governors, St. Bartholomew's Hospital, London, E.C.1, marking envelope "Physicist".

SENIOR LECTURER IN ELECTRICAL POWER, a LECTURER IN ELECTRICAL CIRCUITS AND MACHINES, and an ASSISTANT LECTURER IN ELECTRICAL ENGINEERING—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

The North Staffordshire Field Club. Transactions and Annual Report, 1956–1957. Pp. 118. (Vol. 91.) (Stoke-on-Trent: North Staffordshire Field Club, 1958.) 15*s.* [129

Library Association: North Western Group. Reference and Special Libraries Section. Occasional Papers, No. 1: Library Classification and the Field of Knowledge. By D. J. Foskett. Pp. 15. (London: Library Association, 1958.) 2*s.* 6*d.* [129

Wye College (University of London). Department of Hop Research Annual Report from 1st April, 1957, to 31st March, 1958. Pp. 159. 5*s.* Hop Research at Wye College in 1957. By H. S. Darling. Pp. 5. (Wye: Wye College, University of London, 1958.) [129

Library Association. Special Subject List No. 27: Rubber—Natural and Synthetic. Compiled by E. R. Yescombe. Pp. 10. (London: Library Association, 1958.) 2*s.* 6*d.* [129

Department of Scientific and Industrial Research. Forest Products Research. Special Report No. 13: The Longitudinal Permeability of some Hardwoods and Softwoods. By D. N. Smith and Eleanor Lee. Pp. iii+14. (London: H.M. Stationery Office, 1958.) 1*s.* net. [129

Ministry of Agriculture, Fisheries and Food. Bulletin No. 78: A Selected and Classified List of Books relating to Agriculture, Horticulture, etc., in the Library of the Ministry of Agriculture, Fisheries and Food. Pp. vii+96. (London: H.M. Stationery Office, 1958.) 5*s.* 6*d.* net. [129

Forestry Control in Northern Ireland. Pp. 20. (Belfast: Ministry of Agriculture, 1958.) [129

Empire Cotton Growing Corporation. Progress Reports from Experiment Stations, Season 1956–57. West Indies. By J. R. Spence, C. T. Cave and E. B. Lake. Pp. 10. 1*s.* Kenya. Pp. 14. 1*s.* Survey of Reports. By D. F. Ruston. Pp. 12. 1*s.* (London: Empire Cotton Growing Corporation, 1958.) [129

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